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FUNCTIONAL RESULTS OF CROSSING NERVES AND TRANSPOSING MUSCLES IN THE FORE AND HIND LIMBS OF THE RAT

A DISSERTATION SUBMITTED TO THE FACULTY OF THE DIVISION OF THE BIOLOGICAL SCIENCES IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF ZOÖLOGY
1941

By
ROGER WOLCOTT SPERRY

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THE FUNCTIONAL RESULTS OF MUSCLE TRANSPOSITION IN THE HIND LIMB OF THE RAT

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SIX FIGURES

Most of our knowledge concerning the functional adjustment of transposed muscles is derived from cases of muscle transposition for the correction of motor paralyses in the limbs of human beings. The investigation of these clinical cases which has been confined primarily to the question simply of whether readjustment is or is not possible has brought forth the following principles, as formulated by Scherb ('38), regarding the possibility of reeducation after muscle transposition.

In the arm learning follows the transposition of any muscle to compensate for any other non-synergic muscle, provided the operation is mechanically successful. In the leg learning is likewise universal for slow voluntary movements. But for automatic walking movements, reeducation after a muscle is transposed so as to act antagonistically to its normal function may be prevented reflexly by the remaining function of any muscle of the group for which the transposed muscle is supposed to compensate. Even in the case of walking movements, however, learning can be expected to follow if all of the muscles

[1] This research was done under the direction of Dr. Paul Weiss in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The motion pictures were taken by Doctor Weiss and their cost was borne by grants from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of The University of Chicago and the Penrose Fund of The American Philosophical Society.

A preliminary report appeared in Anat. Rec., vol. 75, suppl. p. 51, 1939; the motion pictures were demonstrated at the meetings of the American Society of Zoologists at Columbus, Ohio, December, 1939.

for which the transposed muscle is substituted are completely paralyzed.

Extremely little is known about functional adjustment of transposed muscles in the common laboratory animals. Marina ('12) reported that after transplanting the insertions of opposing pairs of ocular muscles in monkeys there was an immediate adjustment in the action of the transposed muscles to produce coordinated eye movement. Olmsted, Margutti, Yanagisana ('36) repeated the experiment on cats, dogs, and monkeys, and also reported a rapid functional adjustment which they interpreted as being due to a short training period. Dusser de Barenne and de Kleyn ('29) found that four out of eight rabbits displayed normal horizontal and vertical nystagmus movements of the eye immediately after transposition of the internal and external rectus muscles. They did not attribute this to a functional adjustment, however, since they found further that after excision of all six ocular muscles the remaining retractor bulbi muscle alone was capable of effecting these movements.

Anokhin ('35) states that after transplanting part of the M. extensor quadriceps femoris to a flexor position in the hind leg of the cat, the transposed portion of the muscle, as indicated by the cat's walking coordination, changed its function to a flexor, but that when the muscle was prepared after 5 months training for kymographic recording, the transplanted portion on reflex stimulation contracted synergically with its counterpart as a normal extensor. He interpreted the adjustment as being due to a "dynamic rearrangement" rather than to a fixed change in central nervous relations. Taylor ('36) crossed the Achilles tendons between the hind legs of the frog and contradicted Manigk's ('34) earlier report on the same experiment in saying that there was no immediate adaptation in the function of the crossed muscles. He also sewed the Achilles tendon to a flexor position in the same leg and found no immediate adjustment. The frogs were not kept to determine whether or not a change would occur in time.

The above reports on the effect of muscle transposition thus vary on two points: first, in regard to whether functional adjustment does or does not occur, and secondly, if it does occur, whether it follows gradually as the result of a learning process or whether it occurs immediately by means of automatic reflex accommodation.

A number of cases (Flourens, 1842; Osborn and Kilvington, '10; Rawa, 1885) in which the cross-suturing of nerves to antagonistic groups of muscles in the limbs of dogs, pigs, cats, rabbits, fowls, and guinea pigs resulted apparently in a gradual return to normal coordination might be taken to indicate that the experimentally reversed functional relationship of antagonistic muscles is readjusted by means of learning in these animals. Kennedy ('14), on the other hand, states that restoration of function occurred at once after crossing nerves to flexor and extensor muscles in the foreleg of the dog without any evidence of a reeducation period. The work of Weiss ('36 b), however, has shown that the return of normal coordination after the crossing of limb nerves in amphibians is a phenomenon quite different from either learning or automatic reflex adjustment. In the absence of more conclusive evidence that the same is not also true of the higher vertebrates, one cannot be sure that the effect of nerve crossing is comparable to that of muscle crossing as a criterion of learning or reflex adjustment.

Because of the scarcity and inconsistent interpretation of data on the functional results of nerve and muscle crossing in mammals, and the important implications of such data for the analysis of central nervous function, a reinvestigation of the problem was undertaken, using the rat and creating conditions more critical than previously attempted in the laboratory or obtainable in clinical studies. This paper deals primarily with muscle transposition, cases of nerve crossing being mentioned only as mechanical controls.

Antagonistic flexor and extensor muscles of the hind foot were transposed to discover whether or not there would be an immediate adjustment in coordination on recovery, and if not,

whether adjustment might be brought about in time as a result of reeducation. The albino rat was used because of the large amount of information already available on the behavior and learning capacities of this animal.

The antagonistic muscles of the shank causing plantar and dorsi-flexion of the foot were chosen for study because their normal function is clearly antagonistic and their contraction produces a simple movement that is easily observed, frequently and indispensably involved in the animal's general activity, and readily subjected to natural training situations. Furthermore, since the nerves and nerve tracts concerned are relatively accessible, any adjustment that might occur would be open to further analysis by means of deafferentation, cord transection, and brain stimulation and excision.

THE OPERATION

The tendons of the two main dorsi-flexors of the foot, the M. tibialis anterior and the M. extensor digitorum longus, were cut and inserted together onto the Achilles tendon of the heel so that in their new position contraction of the muscles produced plantar flexion instead of dorsi-flexion. In order to provide more room for these muscles in their crossed position, the small fibula bone and the interosseous membrane were removed entire. The large lateral gastrocnemius muscle inserting normally on the Achilles tendon and producing plantar flexion of the foot was pulled forward, its tendon cut and sutured to the distal end of the extensor digitorum longus tendon so that its contraction in this position caused dorsi-flexion of the foot instead of plantar flexion. The diagrams in figure 1 indicate the essential part of the operation.

Every other muscle of the shank except the M. peroneus longus was removed as follows: After freeing the individual tendons distally and cutting them low down in the ankle, the muscles were pulled proximally and separated cleanly from the surrounding tissues. Then after cutting their nerves and blood vessels and severing the muscles from their origins the entire muscles were lifted out. In this way all the main nerves

and blood vessels in the leg and foot were left intact except those supplying the extirpated muscles.

The M. peroneus longus was left in place between the transposed muscles to help prevent adhesions between them. Its action is mainly that of eversion and does not obscure the reversed plantar- and dorsi-flexor action of the transposed muscles. But because of Scherb's statement that the action of a single remaining antagonist muscle may reflexly inhibit reeducation, the M. peroneus longus was also removed in all

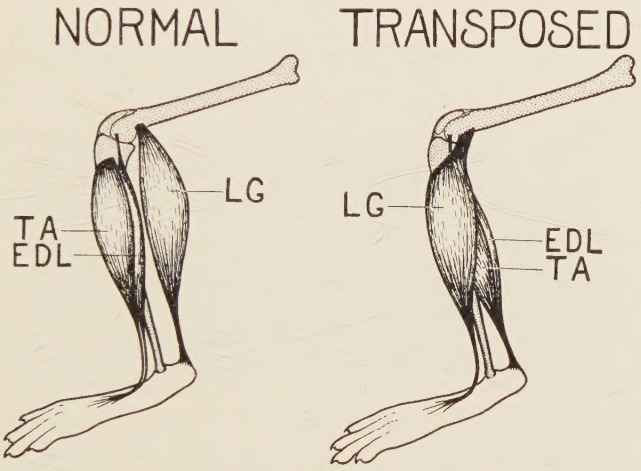


Fig. 1 Diagram illustrating the transposition of flexor and extensor muscles of the foot to produce reversal of foot movement. TA, M. tibialis anterior; EDL, M. extensor digitorum longus; LG, M. gastrocnemius lateralis.

cases by a second operation after the first had healed. This removal of all associated shank muscles thus presents the best condition for readjustment, and also clarifies for study the action of the transposed muscles.

The operations were all performed under sodium amytal anesthesia with a single lateral incision from the upper thigh down to the ankle. The tendons were sutured with fine silk thread. Silk thread was also used in sewing the lateral gastrocnemius muscle to the fascia along the proximal part of the tibia bone to hold it in place and in suturing together the

fascia of the biceps femoris muscle which it is necessary to cut in the operation.

RECOVERY

On coming out of the anesthesia the animals held the operated leg behind them off the floor. After a few days when the swelling caused by the operation had subsided, the leg was held in a more normal position and some weight was put on it. In about 2½ weeks, depending on the neatness of the tendon sutures and the age of the animal, the foot began to show active movements which gradually became stronger. These movements from the beginning were in the reversed direction.

It soon became obvious that rapid recovery of normal co-ordination as reported for transposed ocular muscles, does not occur in these transposed limb muscles of the rat. After complete healing and regeneration of the tendon, pinching of the toes to elicit the withdrawal reflex produced flexion of the hip and knee joints as usual but plantar flexion of the foot instead of the normal dorsi-flexion (see fig. 4 b). When the rats tried to lift the foot in walking, the foot instead of rising with the knee, jerked downward so that the toes scraped along the floor. In the supporting phase of locomotion when the foot would normally be somewhat flexed in the plantar direction to support the weight on the toes with the heel off the floor, the foot was flexed dorsally with toes up in the air and the weight back on the heel (see fig. 6 b). When the animals attempted to rise upright on their hind legs and toes, they went back on their heels and the toes swung up in the air (fig. 5 b). When, in climbing, they tried to dorsi-flex the foot forward and upward, the foot extended downward and backward in extreme plantar flexion (fig. 2 b)—and so on, all the normal active movements of plantar and dorsi-flexion of the foot were in reverse.

In a number of the animals there was no recovery or only partial recovery of foot movement due to adhesions, ankylosis, slipping of the silk sutures, etc. These animals were all dis-

carded and only the nine rats to be described here, showing complete free movement of the joint through approximately the normal 170 degrees, were retained to determine whether or not the reversed foot movement could in time be adaptively modified by reeducation.

The further history of the leg movement in these animals can be summed up briefly here in saying that there was no sign of any functional adjustment whatever in the action of the transposed muscles. In view of the literature on muscle transposition in man and that on the cross suturing of nerves in the hind limbs of lower mammals, it was somewhat surprising to find that the reversed movements in these rats persisted

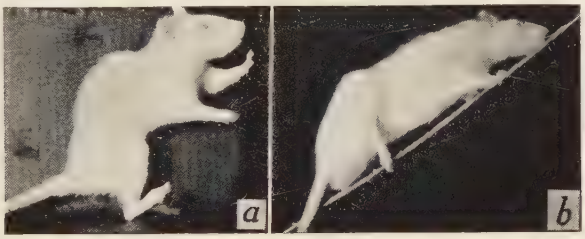


Fig. 2 Photographs showing foot posture resulting from reversed action of transposed muscles.

(a) When anti-gravity muscles of the leg contract to support the animal's weight, the foot, instead of pressing downward against the floor, flexes dorsally.

(b) When leg is lifted upward in climbing, instead of rising upward and forward with the knee, the foot pulls downward and backward in extreme plantar flexion.

without change, that the rats were incapable of learning not only to use the transposed muscles to advantage but even to inhibit the old contraction patterns which, with the muscles in the crossed position, were a distinct hindrance in much of their activity. Although six of the rats were kept longer than 13 months after the operation, readjustment failed to occur either in locomotion and other common activities, or under various training conditions calling for single, slow, elementary foot movement.

TESTS

Nine rats (seven unilateral and two bilateral cases) were obtained which showed on recovery unrestricted movement of the operated foot. The youngest was operated at the age of 50 days, the others at ages ranging from 55 days to 12 months. No age difference appeared in the results.

The reversed coordinations were tested in a series of twelve specific reactions involving dorsi-flexion and plantar flexion of the foot. These reactions were reliably consistent in normal animals. Also in control animals (operated similarly to the experimental group with removal of all shank muscles except the lateral gastrocnemius and extensor digitorum longus which were left uncrossed) these test reactions were likewise consistent and very similar to the coordination of normal rats.

The following movements described as they occur in normal and control rats were used as tests for contraction of dorsi-flexor muscles: (1) Raising and bringing forward of the foot during the suspended phase of locomotion (fig. 6 a). (2) Withdrawal reflex in which the foot is pulled upward when the toes are pinched or pricked (fig. 4 a). (3) Holding of the foot in a flexed position during the scratch reflex. (4) Extreme

Fig. 3 Foot posture when rat is held up by the forequarters with hind foot just touching the floor. (a) Control, operated as for muscle transposition save that muscles were left uncrossed. (b) Muscles transposed. (c) Muscles transposed and nerves to the muscles crossed.

Contraction of the lateral gastrocnemius muscle produces plantar flexion of the foot in (a) and dorsi-flexion in (b). In (c) the nerve of the gastrocnemius muscle activates the anter. tibial and ext. dig. longus muscles whose transposed tendons produce plantar flexion of the foot.

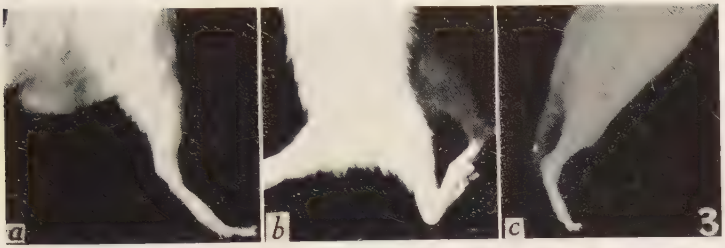
Fig. 4 Withdrawal reflex. (a), (b), and (c) as in figure 3.

The normal dorsi-flexion shown in (a) is reversed to plantar flexion after muscle transposition in (b) and counter-reversed back to dorsi-flexion again in (c) by the double operation in which the nerves are crossed as well as the muscles.

Taken from consecutive frames of motion picture film at 24 frames per second.

Fig. 5 Rising upright on the hind legs. (a), (b), and (c) as in figure 3.

Animals normally rise on toes and ball of the foot as in (a). In (b) the plantar flexion is reversed to dorsi-flexion so that the toes point up in the air and the weight falls on the back of the heel. In (c) the muscles somewhat weakened by incomplete reinnervation after nerve crossing do not lift the heel entirely off the floor as in (a), but if the body weight is somewhat lessened by partially lifting the animal as in figure 3 c the foot shows pronounced plantar flexion.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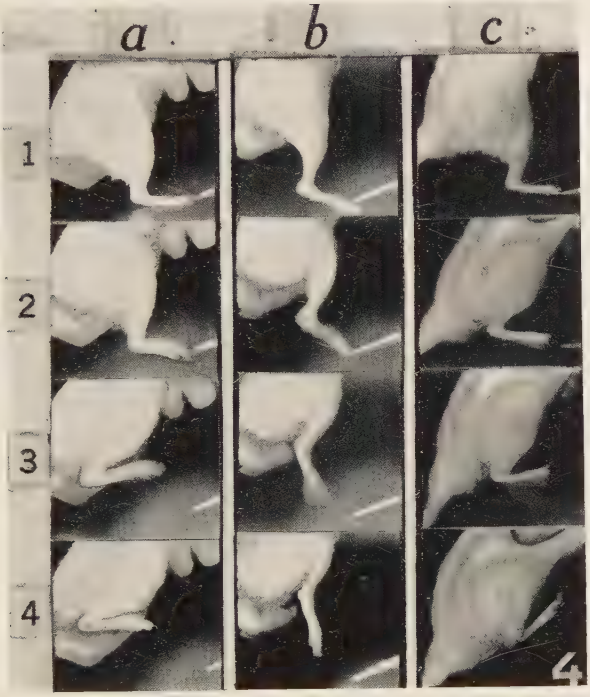
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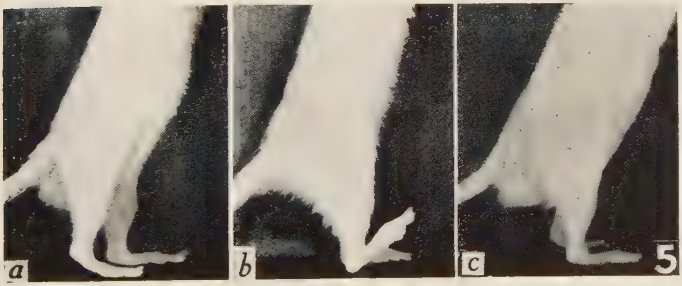
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lifting of the foot to clear an obstacle over which the animal is moving. (5) Escape movements when the rat is held down on its back by pressing across the abdomen. The foot is dorsi-flexed and brought forward underneath the restraining fingers. (6) Lifting of the foot in climbing a ladder, up the sides of the wire mesh cages, or over the edge of a wall.

In all of these reactions contraction of the dorsi-flexor muscles predominates over that of the plantar flexors resulting in dorsi-flexion of the foot. After transposition the muscles contract as before producing plantar flexion in the above tests instead of dorsi-flexion (figs. 2 b, 4 b, and 6 b).

The following responses shown by normal and control rats were used to test for contraction of the gastrocnemius muscle: (1) Supporting of the body weight on the toes and ball of the foot and pushing forward during the supporting phase of locomotion (fig. 6 a). (2) Placing of the foot when the rat is held upright by the forequarters with the hind foot just touching the floor. The foot is plantar-flexed, keeping the toes in contact with the floor (fig. 3 a). (3) Holding of the foot in a position to support the body weight when it is shifted to the hind feet in climbing a ladder and up the sides of the cages. (4) Braking action of the hind foot when the rat is dragged by the front legs slowly forward across the floor. The foot is pressed firmly against the floor and digs in if the substrate is soft. (5) Rising upright on the hind legs with the heels

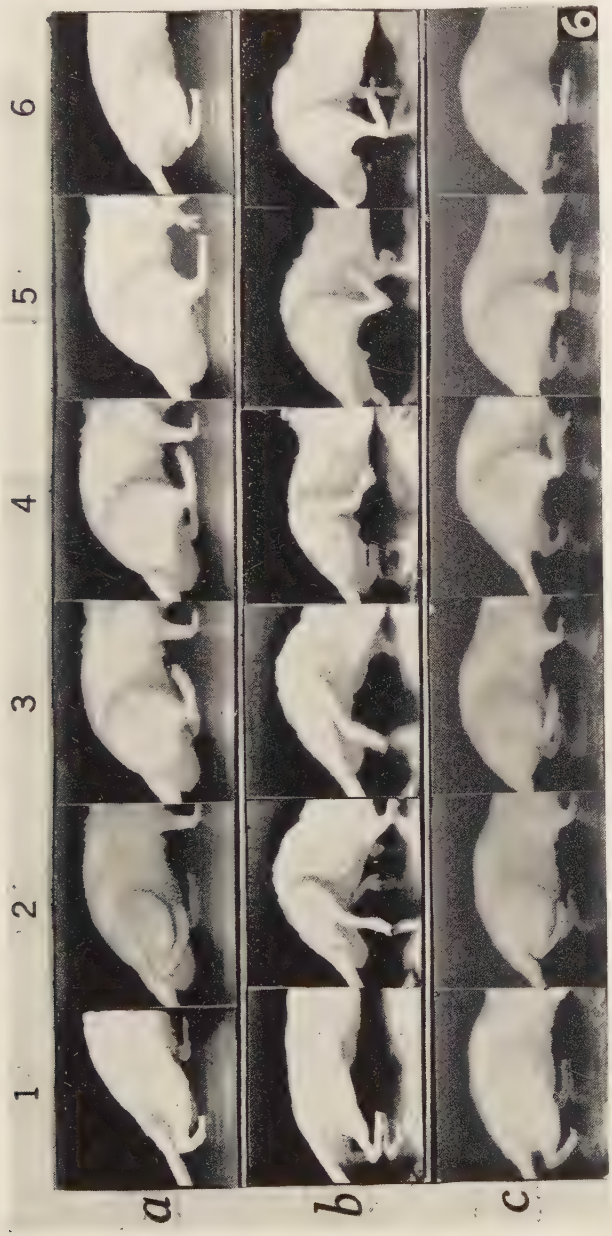
Fig. 6 Locomotion.

(a) Control, operated as for muscle transposition save that muscles were left uncrossed. As the knee is raised and brought forward the foot rises with it. When the animal's weight is shifted onto the foot in the supporting phase of the cycle, the foot is pressed downward against the floor.

(b) Muscles transposed. The foot, instead of rising with the knee, pulls downward and scrapes along the floor. In the supporting phase of the cycle, instead of pressing downward, the foot swings upward so that the weight falls on the back of the heel with the toes pointing up.

(c) Muscles transposed and nerves to muscles crossed. As in (a) the foot is dorsi-flexed in the suspended phase of the cycle and plantar-flexed against the floor in the supporting phase.

Figures taken from two successive cycles of locomotion. Where a rapid phase of the movement was blurred in the main cycle, a corresponding frame from the succeeding cycle was substituted.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off the floor and the body weight on the toes and ball of the foot (fig. 5 a). (6) Resting with the weight entirely on the hind legs while eating, cleaning, etc. The foot is pressed firmly flat against the floor.

In some of these tests, as in (3) and (6), the posture of the foot may be one of slight dorsi-flexion, but actually the gastrocnemius is contracting more powerfully than the dorsi-flexors to support the body against gravity. After transposition the gastrocnemius continues to contract in all of these tests causing a dorsi-flexion of the foot with the toes and ball of the foot swinging upward instead of pressing downward (figs. 2 a, 3 b, 5 b, and 6 b).

The rats were put through these test movements once a week for the first 2 months and monthly thereafter. Besides these test observations, considerable time was spent studying the rats' general activity in their cages, particularly their conduct in the special training situations. Moving pictures taken of locomotion and of some of the test reactions about 2 weeks after the return of function were compared with pictures taken 1 year later.

CHECKS AND CONTROLS

Clinical studies along with the work of Stewart ('37) have shown that disturbances in the muscle pattern produced by foreign innervation, paralysis, and tendon section can be compensated for, to a surprising degree, by so-called "trick movements" of associated muscles still in their normal condition. In the present cases this complicating factor was eliminated by complete removal of all the other muscles acting on the joint.

The reversal was not a passive movement produced by accessory tendons, fascia, pulling of the skin, or other mechanical factors. It disappeared after cutting the nerves or tendons of the transposed muscles. It did not occur on passive extension and flexion of the knee by manipulation under light anesthesia. The lateral gastrocnemius muscle is a two-joint muscle and is so attached in the normal animal that extension

of the knee results in passive plantar flexion of the foot. The possibility that extension of the knee might cause a passive dorsi-flexion of the foot after the muscle had been transposed was tested by mechanically extending and flexing the knee of the operated animals under light anesthesia. In no case did even extreme extension of the knee cause dorsi-flexion of the foot. In three cases it brought the foot into a neutral position at about right angles to the shank, but the foot was loose enough in these cases to be easily plantar-flexed with slight pressure. The two-joint action of the lateral gastrocnemius muscle had been successfully suppressed by fastening the proximal end of the muscle to the tibia bone in the operation (see fig. 1). The extensor digitorum longus is also a two-joint muscle, but the leverage effect on the origin is negligible so that passive flexion of the knee had no effect on foot posture. The possibility that knee action was exerting a slight pull on the muscles which, though not strong enough to manifest itself in actual movement of the foot, was enough to excite stretch reflexes and was thus producing the reversed movement, was tested by deafferentation. In the case so tested the reversal was unaffected by deafferentation of the limb. One of the three cases mentioned in which the passive pull of the gastrocnemius was noticeable when the knee was fully extended was reoperated and the origin of the gastrocnemius on the femur was severed and sutured to the fascia along the proximal end of the tibia thus making a one-joint muscle of the gastrocnemius. On recovery, the reversal continued as before until the rat's death 5 months later.

The reversal was not caused by an abnormal disbalance in muscle strength. It consisted of clear-cut reciprocal movements showing agonist contraction and antagonist relaxation as indicated by the following: The movement occurred distinctly in both directions, full plantar flexion and full dorsi-flexion appearing in turn in exactly the opposite phase in which they appeared in the normal controls. In cases where one of the muscles slipped loose and was removed leaving only one transposed muscle in place, then instead of a persistent

generalized flexion of the foot by the one muscle there occurred distinct active movement in one direction only with the foot hanging limp during the phase in which the missing muscle would have been contracting. Using two transposed muscles for plantar flexion to oppose only one for dorsi-flexion tended to maintain the normal strength relationship. Moreover, the leg of one control animal from which all the plantar-flexor muscles were removed except the small soleus muscle, which constitutes less than one-fifteenth the total mass of the plantar flexors and about one-fifth the mass of the transposed dorsi-flexors, was found to have fair coordination in the normal phase despite the extreme disbalance in muscle strength.

The crossed muscles were sufficiently strong to be used to advantage in normal coordination. That the crossed lateral gastrocnemius muscle was quite strong enough to produce dorsi-flexion is obvious because it did produce such movements. That the tibialis and the extensor digitorum combination was strong enough to support the weight of the rats is indicated by the fact that in control animals the single lateral gastrocnemius, somewhat less in mass than the combined tibialis anticus and extensor digitorum muscles, was sufficiently strong to raise the rat well off its heels when it rose upright on its hind legs. Even the small soleus muscle was capable of raising the heel off the floor in locomotion. Post mortem dissection of the rats showed that there had been no noticeable atrophy of the muscles and that they had been well adjusted so as to exert pull on the Achilles tendon during contraction. But even had the muscles been too weak to completely support the animals, one would still expect, had learning been possible, that there would have been some inhibition of the old contraction patterns which were more disadvantageous than no movement at all.

Tests for sensitivity several weeks after the return of function of the transposed muscles, along with dissection showed that the operations had been successful in preserving the nerve supply of the leg and foot. Slight pricking and pinching of the skin in all regions of the shank, foot, and toes

produced reflex reactions. Pressing the foot and bending the toes also caused reflex reactions. There was a small area in the ankle just anterior to the incision which in some cases was insensitive, but when tested 5 months later it too had regained its sensitivity. In two cases the incisions were opened 8 months after the operation. Reflex responses were elicited under light anesthesia by pinching the crossed muscles and even the tendons at the point of suture.

NERVE CROSS CONTROL

In one animal the nerves were crossed instead of the muscles, operation otherwise similar. The result was the typical reversal of foot movement characteristic of muscle transposition. In this control the reversal of foot movement was produced by a reversal of the sequence in which the muscles contracted without changing the insertions or otherwise altering the anatomical arrangement of the muscles. The dorsi-flexor nerves discharged into the plantar-flexor muscles at the time when dorsi-flexion normally would have occurred, and the plantar-flexor nerves activated the dorsi-flexor muscles when plantar flexion would normally have occurred. The retention of the nerve's original incidence of discharge for some time after regeneration into a foreign muscle is taken to be similar to that which occurs in adult amphibians as contrasted with the muscle-specific changes characteristic of younger animals (Weiss, '36 b).

CONTROLS WITH BOTH NERVES AND MUSCLES CROSSED IN THE SAME LEG

Finally a crucial test was made to show that the muscles in the transposed position were mechanically capable of producing the normal effects given the proper timing in their contraction. Two rats were prepared in which the nerves to the appropriate muscles were crossed and after allowing time for regeneration of the nerves, the regular muscle transposition was performed in a second operation. As a result of the counter-reversal these animals showed on recovery good

plantar flexion and dorsi-flexion of the foot in normal phase in all of the test reactions (see figs. 3 c, 4 c, 5 c, and 6 c). The double negative gave a positive effect. Reversing the action of the muscles without changing the incidence of their contraction reversed the foot movement, but when both the mechanical action and the timing of the muscles were changed to that of their antagonists by transposition plus nerve-crossing, then the transposed muscles worked just like the antagonists which they had replaced, resulting in normal coordination. These two control cases in which the foot was flexed and extended in normal phase to the animal's advantage by muscles transposed exactly as in the nine experimental animals showed conclusively that it was not any anatomical or mechanical aspect of the operation that was preventing readjustment. The lack of adjustment was apparently attributable only to a failure of the nervous mechanisms involved to undergo the necessary changes.

CONTROLS WITH ASSOCIATED MUSCLES LEFT INTACT

To make sure that readjustment would not occur if the associated muscles were left in place, two controls were prepared in which the anterior tibial muscle was transposed to the Achilles tendon and the lateral gastrocnemius was transposed to the extensor digitorum longus tendon and all other muscles of the shank were left intact except three small peroneal muscles, per. brevis, per. digiti quarti, and per. digiti quinti which it was necessary to remove to make room for the crossed tibial muscle. The intact muscles in these rats were strong enough to overpower the transposed muscles so that, although the foot movements were somewhat stiff and of less amplitude than normal, they were closer to normal than to reversed action.

That no adjustment of the transposed muscles occurred was indicated by the fact that after 3 months a partial ankylosis had set in due to the restricted movement of the joint. The legs were reoperated 6 months after the first operation and associated muscles removed to see if the reversed muscles

had undergone any adjustment in their action. In one case the tendon of the lateral gastrocnemius had become so encased to the tibia bone that it was immovable. In the other case the foot movements after recovery from the second operation were in reverse within the narrow limits of movement of about 40 degrees permitted by the partial ankylosis.

Another control was prepared in which all dorsi-flexor muscles were excised and the lateral gastrocnemius transposed to substitute for them, all other muscles being left intact. In this case readjustment would have required dissociation of the action of the lateral gastrocnemius from the other plantar flexors of the shank. As in the two controls above, the intact muscles over powered the transposed muscle so that it was mechanically lengthened in the correct phase of the coordination. The passive pull offered by the tonus of the transposed muscle kept the foot in a more normal posture than in cases where no opposing muscle was present. In a sudden shift from strong contraction of the plantar flexors to complete relaxation as may occur in the withdrawal reflex, the tonus of the transposed muscle brought the foot to a neutral position from extreme plantar flexion so that at first sight it appeared like active dorsi-flexion, but the presence of associated shank muscles and the mechanical lengthening of the transposed muscle in the correct phase of the movement had not resulted in any active adjustment after 6 months.

TRAINING

At first all nine rats were merely allowed to run about in their cages as usual in the hope that learning would occur without any special training. They were kept in groups of two to four in wire mesh cages measuring 45 by 63 cm. and 33 cm. in height, containing sawdust and excelsior. To make the rats more dependent on the operated legs, the contralateral hind foot (except in the two bilateral cases) was immobilized in a position of slight dorsi-flexion by operations causing adhesions and eventual ankylosis of the joint. According to Scherb ('38) any condition that tends to break up the

inherent automatic walking pattern is helpful in bringing about voluntary control over transposed leg muscles.

As they moved about, the animals often paused with the foot in a supporting position, but always on extension of the hip and knee joints the toes would swing upward and the weight fall on the heel. In climbing through the excelsior the rats often caught the operated foot so that they had to stop and make special efforts to free it. The hind feet moved while the animals were licking them, and in the general course of their scratching, feeding, and playing about, all kinds of passive satisfactory and active unsatisfactory movement occurred which offered plenty of trial and error cues for the guidance of learning had the animals been capable of it.

When no improvement appeared in any of the animals after 2 months, special measures were taken to help induce reeducation. An attempt was made to train four of the animals to raise themselves off their heels with the transposed dorsi-flexors by placing food high in the cage where they would have to rise upright on their hind legs to reach it. Hard food was placed in a self-feeder against a smooth wall so that the front feet could not aid in reaching it. The food was raised gradually to a point so high that by resting on their heels and stretching upward to their utmost the rats could just barely nibble at it. It would have been greatly to the animals' advantage to have used the transposed muscles to raise themselves just $\frac{1}{2}$ cm. higher to ease the strain on the rest of the musculature and permit them to get a good bite of the food. Had they been able merely to bring the toes down to the floor and balance on the sole of the foot, it would have given them a firmer footing. But after $3\frac{1}{2}$ months of this training not one of the animals had learned to rise off its heel or to keep its foot flat on the floor. Figure 5 b shows the typical foot posture shown by the rats in rising upright for food. It was a common thing for the rats to balance on the contralateral heel and flex slightly the hip and knee of the operated leg in a sort of climbing movement. The foot was thus brought into a position of plantar flexion in contact with

the floor correctly placed for rising on the toes. The foot might remain there for some time with occasional slight movements as the rat stretched upward. It looked like a good start for learning, but every time the weight was shifted to this leg with contraction of the extensor muscles of the knee, the foot was dorsi-flexed and the toes swung upward. The control animals mentioned above with only two uncrossed muscles in the shank, one for plantar and one for dorsi-flexion, rose easily on their toes under the same conditions (fig. 5 a). Controls with both nerves and muscles crossed in the same leg always rose with the ball and toes of the foot flat against the floor, occasionally lifting the heels well off the floor, when most of the weight was on the contralateral foot (fig. 5 c).

In a further attempt to induce learning, the forelimbs of three of the experimental animals were amputated. According to Bethe ('31) dogs show a remarkable adjustment in the hind limb coordination when the front legs are amputated, an adjustment that does not occur when the limbs are only mechanically immobilized by strapping them to the sides of the body. It was hoped that some adjustment would occur in the transposed muscles when the rats became utterly dependent upon the hind legs for locomotion. Although it was extremely awkward for the animals to have to balance on the points of their heels, they never learned to contract the transposed dorsi-flexor muscles simultaneously with the extensors of the leg. Two of these rats were of a group that had been trained on the self-feeder and the other had been left for 6 months after recovery from the operation without special training. Control animals with forelimbs amputated and only two muscles left in the shank got along considerably better by balancing on the full plantar surface of the foot. The three experimental rats hobbled about without any change in the function of the transposed muscles till their deaths 7, 8 and 10 months later, respectively.

On two other of the experimetnal animals the contralateral hind leg was amputated about ½ cm. above the ankle. Thus

when the rat leaned on the amputated stump in walking, the hind quarters were not as high off the floor as usual and the other leg which previously had to be raised higher than customary to prevent the plantar-flexed foot from scraping the floor (fig. 6 b), now had to be raised still higher. It was thought that the frequent catching and scraping of the foot on the floor would be a motive for inhibition of the reverse plantar flexion with perhaps a change to dorsi-flexion. Both of these animals had previously been kept without special training, one a little over 3 months, and the other about 6 months after the operation. The first was continued 3 months and then the limb with the muscle transposition was deafferented. Three weeks later the rat chewed off the deafferented foot and was sacrificed. The second animal was kept 8 months after the amputation. Neither showed any adaptive adjustment in the action of the transposed muscles.

In a last attempt to reeducate the rats, a cage was arranged in which they had to climb a vertical ladder 45 cm. high to reach food. The ladder was made of wire 2 mm. in diameter, which is thin enough to make it extremely difficult for the rats to balance with the points of their heels on the rungs. The rats climbed mostly with the front legs and since they had to hang by their paws while feeding, they tired after a few nibbles at the food and backed down to rest. This made it necessary for them to make many trips up and down the ladder for a day's meal. In clambering up and down the ladder, the rats made all sorts of movements with their hind legs and got them into all kinds of positions in and about the rungs, but they found no very satisfactory position in which much weight could be taken up by the hind limbs. Whenever the flat of the foot was placed on a rung and the animal started to shift its weight to this leg with consequent contraction of the extensor muscles, the transposed gastrocnemius muscle contracted causing dorsi-flexion of the foot at an angle so acute that any appreciable downward force applied to the foot caused it to slip off the rung. The rats never learned to rest the ball of the foot on the rungs and contract the

transposed dorsi-flexors at the same time. Control animals with only two antagonistic muscles left in the shank in normal position climbed quite easily by placing the flat of the foot on the rung and contracting the gastrocnemius, thus allowing most of their weight to rest on the hind legs. The controls with both nerves and muscles crossed in the same leg also climbed quite well by contracting the transposed dorsi-flexors synergically with the knee extensors. Of the two experimental animals, one, a bilateral case, was the youngest of the group of nine. The other was also a bilateral case but in one of the legs the lateral gastrocnemius muscle had been removed leaving only the transposed dorsi-flexors for plantar flexion. Both animals had previously been in the group of four trained for 3½ months to rise upright on their hind legs for food. The training on the ladder continued till their deaths 8 and 9 months later, respectively, without any sign of reeducation.

DISCUSSION

No adjustment, either immediate by means of automatic reflex regulation or gradual by means of a learning or conditioning process, appeared in the action of the transposed muscles in these rats.

The only functional adaptation which occurred was adjustment in the contraction of muscles left intact in normal position. For example, the rats avoided scraping the toes of the operated leg in walking, not by modifying the action of the transposed muscles, but by lifting the whole leg higher off the floor with the hip and thigh muscles, at the same time shifting more weight to the front legs. They managed to locate points about the head, neck and upper body while scratching, not by adaptive use of the transposed muscles which kept the foot extended in an unnatural position, but by adjustment of the rest of the musculature to this abnormal foot posture. There were many such adjustments on the part of the intact musculature to compensate for the reversed foot movements but none in the action of the transposed muscles.

The absence of any immediate automatic reflex adjustment in the transposed muscles and the persistence of the reversed movement after deafferentation of the limb indicates a central nervous organization of the basic motor patterns for limb coordination. Locomotion in the rat is not the simple result of a totality of separate myotatic reflexes controlling the individual muscles of the limb according to the mechanical and postural stresses imposed on the limb structure during movement. The spinal cord must contain mechanisms for producing the organized contraction pattern of the limb musculature. Besides the apparatus for reciprocal contraction and relaxation of antagonistic muscles described by Sherrington ('06), the nerve centers must also contain a mechanism for synchronizing the contraction of shank, thigh, and hip muscles. The hind limb of the rat is generally moved as a whole, not in separate segments, and when the muscles of the shank are transposed, the rat is unable to alter the functional relationship of these muscles in the whole limb pattern. Stimuli from the periphery play upon the central mechanisms to start, stop, and modify in intensity the motor discharges to the limb, but the basic pattern of these discharges to the limb musculature depends in large part on central factors. This interpretation is in accordance with the results of studies on limb deafferentation in the rat (Sperry, unpublished) and other vertebrates (Weiss, '36 a).

In regard to the inability of the rats to correct the reversed movements by learning, it may be that rats operated at an age younger than 50 days would be more amenable to re-education after muscle transposition, though according to Liu ('28) the learning capacity of the white rat as measured with mazes is still increasing rapidly during the period from 30 to 75 days, and reaches its maximum at 77 to 100 days. According to the principles derived from the transposition of muscles in the leg of man, the transposition as performed on these rats with removal of all the other muscles acting on the same joint presents the best possible condition for learning.

After muscles for both plantar and dorsi-flexion are transposed, learning does not necessitate a dissociation of function within a group of muscles normally synergic in action as would be the case if, for example, one of the plantar flexors were left in normal position and another crossed over to produce dorsi-flexion. With the crossing of muscles for both plantar and dorsi-flexion no change in function is required either within a single agonist group of muscles or between the agonist and antagonist groups. The only change necessary is a shift in the normal functional tie-up between the shank muscles as a group and the rest of the leg musculature. Perhaps the simplest condition for learning was represented in that case in which the lateral gastrocnemius muscle was removed leaving only the dorsi-flexors to be adjusted.

Inability of the rat to modify the reversed hind foot movement as contrasted with the experience of human beings seems best attributed to the primitive condition of the rat's central nervous system. Weiss ('36 b) has shown that in amphibians, movements of the entire limb are stereotyped in relation to body movement and are not subject to learning adjustment. On the other hand, in man (Scherb, '38) the action of a single synergic group of muscles in the shank can be dissociated after muscle transposition by reeducation. There is thus an increase in capacity to modify by learning the fundamental motor patterns of limb coordination in passing from the lower to higher vertebrate forms. Clinical studies also indicate an increase in this capacity in passing from the hind limb to the fore limb in man.

Reversal of the functional relationship between the muscles of the shank and those of the rest of the limb would presuppose dissociation and reintegration of a fundamental motor pattern. Apparently, the brain processes involved in learning can deal with this pattern only as a unit. Such a unit can be combined with others in different ways to produce new behavior patterns in the gross, but finer and more extreme modifications of behavior requiring alterations of the basic units themselves, such as reversal of the inherent functional relations between

antagonistic muscles of the limb, cannot be made by the rat. Learning as observed in the behavior of the rat in mazes, problem boxes, ladders, etc., must be the result of a reassociation of these unmodifiable functional entities and higher units into new combinations and not the formation of totally new reaction patterns. The unmodifiability of these basic central nervous processes for hind limb coordination furnishes further support to the view that the process of habit formation is hierarchical in nature and involves the association of smaller units of behavior which are already organized (Weiss, '37).

SUMMARY

1. In nine rats (seven unilateral and two bilateral cases, operated at ages ranging from 50 days to 1 year) transposition of flexor and extensor muscles of the foot produced a reversal of foot movement.

2. As indicated by continued observation and moving picture study the reversal persisted in all cases with no functional adjustment, transitory or prolonged, either in common activities or in special trained performances demanding a single, slow, elementary foot movement.

3. Analysis showed that the reversal was due to clear-cut reciprocal contraction and relaxation of the transposed muscles; that mechanically the transposed muscles were capable of producing normal movement when the nerve discharges were properly timed; and that the sensitivity of the shank, ankle, foot, and transposed muscles and tendons had not been impaired by the operation.

4. A control in which the nerves were crossed instead of the muscles exhibited the same reversal of foot movement that followed muscle transposition. Controls in which both nerves and muscles were crossed in the same leg displayed, as a result of the double reversal, flexion and extension of the foot in the normal phase.

5. The nine experimental rats were kept $15\frac{1}{2}$, $14\frac{1}{2}$, 14, $13\frac{1}{2}$, $13\frac{1}{2}$, 13, 7, 6 and 5 months, respectively, after the operation. Immobilization and amputation of the contralateral hind leg,

similar transposition of muscles in the contralateral hind leg, amputation of both fore legs, training the rats to stretch upright on their hind legs for food for 3½ months as well as to climb a ladder 45 cm. high for food for 8 months, all failed to induce reeducation.

6. The unmodifiability of the elementary contraction patterns of the hind limb musculature and their persistence after deafferentation of the limb is taken to indicate a central nervous organization of the basic motor patterns for limb coordination.

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THE EFFECT OF CROSSING NERVES TO ANTAGONISTIC MUSCLES IN THE HIND LIMB OF THE RAT

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When nerves to limb muscles are forced by operative measures to activate opposing muscles in amphibians, no corresponding disturbance results in the response pattern of the limb muscles (Weiss, '36). Contrary to the view that specific connections between nerve centers and end organs are important in determining the pattern of response, the muscles or limbs so operated contract normally in timing and in intensity regardless of the experimental distortion of their nerve connections. It has been demonstrated further that this return to normal function after crossing of limb nerves in amphibians is not the result of reeducation or of any kind of automatic reflex adjustment (Weiss, '37).

The only tenable explanation of the phenomenon yet suggested is that offered by Weiss himself in terms of modulation of nerve by muscle. When nerve fibers growing out in ontogenetic development make contact with peripheral organs, they are presumably induced by those end organs to undergo a further cell differentiation according to the specific biochemical properties of the end organ. Nerves to different muscles thus become differentiated qualitatively from each other. When a nerve is severed from its muscle and forced to

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regenerate into a foreign muscle, the nerve cells under the influence of the new muscle, undergo a process of cell modulation losing the specific properties induced by the original muscle and acquiring those specific to the new muscle. These specific properties of motor nerves result in selective sensitivity of the nerves of the various muscles to different central excitatory agents. According to the Resonance Principle this selective sensitivity rather than the anatomical connections in the ventral horn, links the individual muscles with their respective central activators. Normal function thus reappears after experimental disarrangement of the peripheral nerve connections as soon as the nerves are modulated by the muscles into which they regenerate. Evidence has been presented that nerves undergo these muscle-specific changes also in embryonic stages of human development (Weiss, '35).

Apparent recovery of normal function after nerve crossing in birds and mammals has in the past been attributed to reeducation or to automatic reflex regulation without testing for other possible factors such as modulation of nerve by muscle. Flourens (1842) crossed the medial and ulnar nerves in the fowl. Rawa (1885) crossed the peroneal and tibial nerves in rabbits, cats, dogs, and pigs. Osborne and Kilvington ('10) crossed the peroneal and tibial nerves in dogs. These investigators all report a restoration of normal function and attribute it to reeducation. Barron ('34) in summarizing the literature concludes that the crosses between spinal nerves have been more successful than those between cranial nerves in being followed by a complete independence of the movements of the muscle groups involved. He made anastomoses between fore and hind limb nerves in the rat and reported that a gradual dissociation of movement occurred as the result of a learning process. Kennedy ('14) after crossing flexor and extensor nerves in the front leg of the dog, states that recovery occurred without any evidence of a training period and that it was probably due to an immediate reflex adjustment to the altered periphery rather than to learning. Although the numerous clinical reports are somewhat controversial, the pre-

dominating opinion in neuro-surgery seems to be that the crossing of limb nerves in human patients results in a corresponding distortion of sensation or response which can be corrected in time by reeducation provided there are not numerous axon bifurcations to non-synergic muscles or to receptors of different modality.

These reports imply a plasticity of the nerve centers that is directly at variance with the results of muscle transposition in rats (Sperry, '40). When flexor and extensor muscles of the hind foot of 50-day-old rats are transposed, a reversal of foot movement follows which persists permanently without the slightest corrective modification. Even after amputation of the front legs and 8 months of special training, the foot action remains unalterably reversed. In view of the fact that foot coordination in these cases proved completely refractory to reeducation, it seems questionable that the ready restoration of apparently normal foot function following nerve crosses in rabbits, cats, dogs, and pigs could actually have been due to learning or reflex regulation. Persistence of the correction in foot movement after cord transection in Osborne and Kilvington's dogs suggests, in itself, that the adjustment was due to some factor other than reeducation, because spinal conditioning has never been conclusively demonstrated elsewhere. Modulation of nerve by muscle is such another factor that would result in recovery of normal function. In amphibians an age difference has been demonstrated; modulation occurs quickly in larval stages but may require as long as several months in older animals (Weiss, '36). A corresponding slow modulation of crossed nerves in post-embryonic mammals would be practically indistinguishable in effect from reeducation.

To date no study has been undertaken to determine for certain whether or not such a modulation process occurs. In the present experiments nerves were crossed in the hind limb of the rat to the same set of muscles which was used previously in muscle transposition for the purpose of (1) comparing the functional effects of nerve crossing and muscle

transposition under similar conditions, and (2) discovering whether the limb nerves of postnatal mammals have become irreversibly determined or are still capable of undergoing muscle-specific changes on regeneration into foreign muscles.

METHOD

A reversal of hind foot movement was produced by crossing nerves to flexor and extensor muscles of the shank. In the previous investigations of other authors on the crossing of limb nerves, large compound nerve trunks have been employed containing fibers to several different groups of muscles as well as a large number of cutaneous and other sensory components. Reeducation was favored and general confusion avoided in the present work by isolating and crossing the pure individual branches to single muscles. All remaining shank muscles, whose nerves were not crossed, were excised. This clarifies, for study, the action of the test muscles and also eliminates reflex inhibition of reeducation by the continued action of shank muscles with normal innervation.

Because both modulation and reeducation result in restoring normal limb function after nerve crossing, critical conditions were established to separate the two factors so that one could clearly tell of any adjustment in function that occurred whether it was due to modulation or to reeducation: Correction of reversed foot movement following the crossing of nerves, when it had been shown not to follow the transposition of the muscles supplied by those nerves, would, in itself, suggest that some factor other than reeducation was responsible. Spinal cord transection should abolish the adjustment if due to learning, but not if due to modulation. Furthermore, by first crossing the nerves and then transposing those muscles supplied by the crossed nerves, a crucial test situation was established under the conditions of which modulation could not possibly be mistaken for reeducation. Foot movement in normal phase is the immediate result on recovery from such a double operation (see Sperry, '40). Subsequent modulation of nerve by muscle would have to show up as a shift from

normal to reversed action which could hardly be interpreted as reeducation.

OPERATION

The nerve branch to the soleus muscle, a plantar flexor, was dissected out carefully back to its emergence from the tibial trunk. The nerve was then cut distally next to the muscle, pulled anteriorly, and inserted into the anterior tibial muscle, a dorsi-flexor, after the original nerve to that muscle had been severed. Similarly, the distal cut end of the nerve to the extensor digitorum longus muscle, a dorsi-flexor, was pulled posteriorly and inserted into the medial gastrocnemius muscle, a plantar flexor, after its original nerve had been severed.

All other shank muscles, whose nerves had not been crossed, were excised. The loose ends of the original nerves to the intact muscles and those of the excised muscles were ligated with fine silk thread and tied to tissues away from the intact muscles to prevent undesired regeneration. The nerves were inserted in the muscles directly at the motor point in an attempt to bring the cut end of the foreign nerve into contact with the distal stump of the original nerve whose degenerating ramifications through the muscle provide pathways for regeneration. More complete reinnervation of the muscle is thus insured than when the insertion is made elsewhere.

Another technique was also used in crossing the nerves in which the cut end of the foreign nerve instead of being inserted directly into the muscle, was sutured to the distal stump of the original nerve. The sutures were tubulated in a small piece of artery obtained from another rat according to the method of Weiss ('41). The artery itself was sufficient to hold the two cut ends of nerve together provided a little slack was allowed in the length of nerve. Extra length when needed was obtained by separating the muscular branch from the main trunk farther proximally after removing the common connective tissue sheath. In anticipation of the operation for muscle transposition to be made on some of the cases after regeneration of the crossed nerves, the nerves were

cross-sutured to the lateral head of the gastrocnemius muscle which is more easily transposed than the medial head.

In a number of the first trials ankylosis of the joint set in before muscular activity was restored by nerve regeneration. It was found preferable to leave the deep plantar flexor muscles intact in the first operation and excise them in a second operation after regeneration of the crossed nerves had taken place. Contraction of the deep plantar flexor muscles maintains the mobility of the joint and helps prevent ankylosis.

The operations were performed under sodium amytal anesthesia with a single lateral incision from above the knee to the ankle. A short incision along the medial side of the tibia bone under ether anesthesia was made for removal of the deep plantar flexor muscles in the second operation.

RECOVERY

After the operation the foot hung limply in those cases in which all the extra muscles had been excised. After a period, varying in different cases from 3½ to 6 weeks, active foot movement began to reappear in the operated limbs. This movement from the start was in reverse. Plantar flexion instead of the normal dorsi-flexion occurred in the withdrawal reflex. When the rats tried to rise upright on their toes, the foot was dorsi-flexed instead of plantar-flexed so that the toes swung up in the air and the body weight fell on the back point of the heel. The reversed action gradually became stronger and occurred regularly in all reflex and spontaneous leg movements.

In the remaining cases the deep plantar flexor muscles were excised at the end of 8 weeks. These rats began to move the foot in reverse a few days after the second operation, as soon as the leg had healed.

Ten successful cases were obtained with complete reversal of hind foot movement unrestricted by ankylosis. In eight of these cases, six unilateral, two bilateral, the nerves had been inserted directly into the muscles. In the remaining two, both

unilateral, the nerves had been cross-sutured in arterial tubes. Two more successful cases were obtained in which the muscles had been transposed 8 weeks after the nerves were cross-sutured. The muscles were transposed and the tendons re-inserted in such position that contraction of the gastrocnemius muscle produced dorsi-flexion of the foot instead of the normal plantar flexion, and contraction of the anterior tibial muscle produced plantar flexion instead of dorsi-flexion. In these animals the reversal of muscle action cancelled the reversal produced by nerve crossing, so that dorsi-flexion and plantar flexion occurred in normal phase in all active leg movement. The twelve cases at the time the nerves were crossed varied in age from 40 to 250 days. No age difference appeared in the results except that there was some indication of more rapid and complete nerve regeneration in the younger animals.

The animals were kept under close observation in large cages with a deep flooring of sawdust to protect the operated feet. Once a week for the first 2 weeks and monthly thereafter, the animals were put through a series of twelve specific test reactions involving plantar flexion and dorsi-flexion of the foot. These reactions included the suspended and supporting phases of locomotion and climbing, the withdrawal reflex, placing reaction, scratch reflex, rising upright on the hind legs, escape movements when the rat is held down on its back by pressing across the abdomen, and braking movements of the hind feet when the rat is pulled forward across the floor by its forequarters. These test reactions furnish a reliable index of the contraction of the shank muscles in both voluntary and reflex activity. They have been described in detail with the corresponding foot movements in normal and in reverse phase (Sperry, '40). Moving pictures of some of the test reactions taken 3 weeks after the appearance of reversed foot movement were compared with pictures of the same reactions taken 1 year later.

RESULTS

Cases tested for modulation of nerve by muscle. Six of the unilateral nerve cross cases were left till their deaths without

further treatment. They were kept 6, 10, 13, 15 and 18 months after the operation, respectively. No adjustment in foot movement appeared. The reversal was fully as vigorous and consistent just before death as at the beginning. Likewise no change occurred in those two special cases in which the muscles supplied by the crossed nerves had also been transposed. Flexion and extension of the foot continued in the normal phases of leg coordination. The foot movements, though slightly weakened by incomplete reinnervation, were very similar to those in controls in which all muscles of the shank had been removed except the lateral gastrocnemius and the anterior tibial. There had been no sign of a shift back toward reversal of foot movement when they were sacrificed 15 months after the operation.

The results in regard to nerve modulation in these cases are clear and may be dispensed with briefly. Modulation of nerve by muscle obviously does not occur in rats of 40 days or older. The motor nerves, already specifically determined by their original muscles, are no longer in a sufficiently labile condition to be respecified by foreign muscles. Consequently, in connection with the problem of possible restoration of function after nerve crossing, modulation of nerve by muscle may be discounted as a factor operating in rats at this age.

Cases in which reeducation was attempted. The reversal of foot movement which follows nerve crossing is quite similar in all respects to the reversal which follows muscle transposition. The factors involved in reeducation after crossing nerves should be very much the same as after transposing the muscles activated by those nerves. It was thought, however, that because the position of the muscles is not changed by nerve crossing the array of proprioceptive and kinesthetic stimuli might possibly be more favorable for reeducation after nerve crossing than after muscle transposition. The two-joint gastrocnemius muscle with its origin on the femur bone is mechanically stretched in normal phase by movement of the knee joint. This normal stretching of the muscle is, in most responses, simply exaggerated after nerve crossing by the re-

versal of foot movement, whereas such mechanical effects of knee action were completely abolished in the muscle transposition experiments by attaching the origin of the gastrocnemius muscle to the tibia bone.

With the purpose of forcing out reeducational correction if possible, special treatment was administered to four cases, two unilateral and two bilateral, in which as indicated by palpation, full reinnervation of the muscles had taken place. In the two unilateral cases the contralateral hind foot was immobilized in a neutral position of slight dorsi-flexion by operations causing adhesions and ankylosis of the joint. Four weeks after the appearance of reversed movement, the front legs of one unilateral and one bilateral case were amputated at the shoulder. Because this operation made the animals entirely dependent on the hind legs for support and for locomotion and provided a continuous condition of training where the alteration demanded for the animals' well-being involved the simple sustained contraction of one muscle and inhibition of its antagonist, this test was considered crucial of the rats' ability to correct by a learning process the reversed foot movement. When these rats tried to support themselves on their hind feet, contraction of the anterior tibial muscle activated by the soleus nerve produced dorsi-flexion of the foot so that the toes and sole of the foot were lifted up in the air. The rats continued to balance and hobble about awkwardly on the back points of their heels with the toes pointing upward. They never learned to bring the toes and ball of the foot down to the floor and use them for support. Forty-nine and 63 days of age at the time of the first operation when the nerves were crossed, these two cases died 17 and 16 months, respectively, after amputation of the front legs without any sign of reeducation.

The other two cases, 40 and 83 days old at the time of the first operation, were compelled to rise upright on their hind legs to obtain food. Hard food which could be gnawed only a small bit at a time from a self-feeder was gradually raised so high that it was almost out of reach. When the rats stretched upright to reach the food, their feet were dorsi-flexed

so that they could not get up off their heels. By straining upward to their utmost they were able only to barely nibble at the food. The animals were watched to see if they would learn to contract the gastrocnemius on rising upright, as rats do normally, and thus raise themselves to a position from which the food would be more accessible. They continued to struggle and strain to reach the food from the back points of their heels without ever learning to contract the gastrocnemius muscle at the correct time or even to inhibit contraction of the anterior tibial muscle which kept the toes and ball of the foot in the air and prevented use of the flat of the foot as an aid in balancing. At the end of 6 months the animals had become quite thin and training was discontinued. Up to the time of their deaths 10½ and 9 months later, the reversal of foot movement persisted without modification. In being unable to correct or even to inhibit the reversal of foot movement which was more of a hindrance to them than no foot movement at all, these rats in which the muscles had been left in normal position and only the nerves crossed, were entirely similar to those previous cases in which the muscles had been transposed.

Checks and controls. Post-mortem dissection showed that nerve regeneration had been as intended. There were no stray fibers to the muscles from the original nerve stumps or from other foreign nerves. In two cases which were showing signs of senility and were ready to be sacrificed, the peroneal and tibial nerves were cut and the distal ends stimulated electrically above the point at which the nerves had been sutured. Stimulation of the peroneal nerve caused strong contraction of the gastrocnemius muscle and none of the anterior tibial muscle, while stimulation of the tibial nerve caused strong contraction of the anterior tibial muscle and none of the gastrocnemius muscle. Since the gastrocnemius muscle is normally supplied by the tibial nerve and the anterior tibial muscle by the peroneal nerve, these physiological tests also showed that nerve regeneration had taken place as intended.

The incision was then closed in one of these cases and the anesthesia removed. After healing, 1 week later, it was obvious that the reversal of foot movement had been completely abolished by cutting the nerves. In an extra case in which the operation had not been successful because the reversed movement occurred only in the plantar direction, dorsi-flexion being absent, dissection revealed that the nerve crossed to the anterior tibial muscle had pulled loose, the nerve to the gastrocnemius muscle remaining intact. From this evidence there was no doubt that the reversed foot movement was caused by active contraction of the muscles to which the nerves had been crossed and not by any extraneous mechanical factors.

In control animals in which all the shank muscles had been removed except the anterior tibial and medial gastrocnemius muscles, these two muscles were strong enough to allow the foot to be used to good advantage in coordination very close to that of the normal rat. Two controls similar to the above except that the nerves were cut and connected again to their original muscles in one case and to muscles of the same action in the other, in the former by suture and in the latter by direct insertion, also showed good coordination in normal phase.

In the experimental group reinnervation of the anterior tibial muscle was sufficient in all cases to cause good strong dorsi-flexion of the foot against gravity. That reinnervation of the gastrocnemius muscle was sufficient to lift the body weight of the rat off its heels was questionable in three cases since at death the muscles were only about one-quarter normal size. In the remainder of the cases reinnervation was more complete and in the cases in which reeducation was attempted, palpation previous to training and post-mortem dissection and weighing indicated no appreciable loss of muscle mass. Strong plantar flexion of the foot in the reverse phase was present in all cases.

That sensory as well as motor nerves had regenerated into the foreign muscles was shown by the fact that pinching the exposed muscles under light anesthesia with a blunt forceps produced reflex responses. Reflex responses elicited by prick-

ing the skin and pulling the hair over all regions of the shank, ankle, and foot, and to flexing the toes and ankle about a month after return of function showed that the operation had not impaired the sensitivity of the limb.

CROSSES BETWEEN PERONEAL AND TIBIAL NERVES

Since regeneration of nerves is unselective (Weiss, '36), the crossing of large nerve trunks such as the peroneal and tibial must result in a random redistribution of the motor fibers of any one muscle of the shank or foot to a large number of foreign muscles. Likewise any one foreign muscle must be reinnervated by a heterogeneous lot of fibers that originally were spread among many different muscles. A similar random dispersal must occur among the sensory fibers. For reeducation or reflex regulation to occur in the face of such confused reinnervation would imply an extreme plasticity, homogeneity, and adaptability on the part of the nerve centers that is directly negated by the results of muscle transposition and nerve crosses between individual muscular nerve branches. The latter results show that contraction of the shank muscles as a group cannot be dissociated in the nerve centers from that of the rest of the leg musculature. It seems improbable that this same dissociation plus the much finer dissociations between different groups of shank and intrinsic foot muscles and even between individual neurons, as would be required after unselective regeneration of the peroneal and tibial nerve trunks, could be made after crossing these nerves. Learning would be simpler presumably after reconnecting the fibers of one muscle directly to another single muscle. However, since reeducational adjustment has been reported to follow the crossing of the compound peroneal and tibial nerve trunks in dogs by Osborne and Kilvington and in dogs, cats, rabbits, and pigs by Rawa, this operation also was performed on a number of rats.

Anatomically the dorsi-flexor muscles of the foot are supplied by the peroneal nerve and the plantar flexors by the tibial nerve. In the normal rat electrical stimulation under

light anesthesia of the distal cut end of the peroneal nerve causes sharp strong dorsi-flexion of the foot. Likewise, stimulation of the tibial nerve causes vigorous clear-cut plantar flexion of the foot.

Twenty cases were prepared. They were operated at ages ranging from 15 to 80 days. After cutting the nerves the proximal end of the peroneal was sutured to the distal end of the tibial and the proximal end of the tibial to the distal end of the peroneal. The sutures were enclosed in artery tubes and, because the nerve trunks lie side by side, a long sheet of beef allantoic membrane (Bauer and Black's "insultoic membrane") was placed between the sutured nerves to prevent cross regeneration of fibers to their original branches.

Regeneration occurred as intended. When the legs were reopened after 2½ months, the two nerve trunks were distinctly separable with no sign of stray fibers crossing from one suture to the other. The shank muscles had regained their full size. After cutting the nerve trunks proximal to the point of suture in three cases, electrical stimulation of the cut ends produced dorsi-flexion when the crossed tibial nerve was stimulated, and plantar flexion when the crossed peroneal nerve was stimulated. Clearly the mass of structures normally supplied by the tibial fibers had been reinnervated by the peroneal fibers, and vice-versa.

Flaccid paralysis with muscular atrophy immediately followed the operation. On regeneration of the nerves with resultant recovery of muscular strength and tonus, the foot was moved abnormally but not in reverse as after crosses between individual muscles. There were no loose free reciprocal movements of the foot. Active dorsi-flexion was never seen. Only when the rats were at rest with the leg muscles relaxed did the foot attain a normal position of dorsi-flexion, passively flexed underneath the animals by the body weight. Whenever leg movement occurred, the foot was held rather stiffly and moved only through varying degrees of plantar flexion. As time went on, the plantar flexion became more predominant. During activity the foot was kept stiffly extended. In the supporting

phase of locomotion the body weight was supported on the digits instead of on the sole of the foot. The result of this rigid plantar flexion in locomotion was to make the leg coordination of the rats similar to that of digitigrade mammals such as the cat, dog and pig. In the rat, however, the toes are long and become permanently curled after the operation so that the rats walked on the dorsal rather than on the plantar surface of the toes.

The reason for the predominance of plantar flexion with curling of the toes and rigidity of the ankle joint is not entirely clear, though the following factors are probably in part responsible. The peroneal and tibial trunks contain, besides fibers to the directly opposed flexor and extensor muscles, fibers to the peroneal group of muscles and to the group of deep flexor muscles and also to all the small muscles intrinsic to the foot which groups probably do not all function in perfect synchrony with the primary plantar and dorsi-flexors. If, for example, the posterior tibial and the short and long peroneal muscles contract during plantar flexion as they apparently do in man (Wright, '28), then, after crossing their fibers along with those of the dorsi-flexors into the plantar flexor muscles, one would expect to get a continuous plantar-flexor contraction persisting through both phases of locomotion. Also, because the plantar flexors are much more powerful than the dorsi-flexors, any generalized pull on all muscles produced by prolonged contraction, contracture, or even by muscle tonus, after disruption of the myotatic reflex mechanisms for controlling that tonus, would tend to result in predomination of plantar flexion. Whether cause or result, there was an anatomical shortening of the plantar flexor muscles. This shortening was not so severe in the majority of cases as to prevent reeducational adjustment since good dorsi-flexion of the foot could be obtained by electrical stimulation of the nerve. In most of those cases operated at about 15 days of age, however, when growth is still very rapid, the condition became so severe that complete dorsi-flexion was impossible even by forcible manipulation.

The leg coordination following the crossing of peroneal and tibial nerves was quite similar in all twenty rats save for the age difference mentioned above. Fifteen of the animals were kept longer than a year, nine of them as long as 18 months after the operation. Foot movement remained abnormal to the end with no evidence of correction.

One must conclude either that the nervous system of cats, dogs, rabbits, and pigs is considerably more efficient in regard to reeducation than that of rats, which seems very unlikely particularly in the case of pigs whose central nervous system is decidedly more primitive (Kappers, Huber and Crosby, '36), or that the adjustment observed in these other animals was actually due to anatomical and mechanical peripheral effects rather than to central adjustment. In this regard it should be noted that passive extension of a dog's, cat's, rabbit's, or pig's knee mechanically forces an extension of the foot because of the pronounced two-joint action of the plantar-flexor muscles. Dorsi-flexion is mechanically impossible with the knee extended and can occur only, as it does normally, when the knee is flexed. After crossing peroneal and tibial nerves, knee movement which is unaffected by the operation would thus tend on regeneration of the nerves to control foot movement mechanically as the two-joint muscles gradually recovered their strength and tonus. The effects observed after crossing the peroneal and tibial nerves in the rat, obviously not normal in this animal, would be functionally very adaptive in a short-toed digitigrade animal, and might easily be mistaken for a restoration of normal coordination.

There was no indication of nerve modulation in these cases. Unfortunately the effect of modulation of the few fibers that had not yet reached their end-organs at the time of operation in the youngest animals would have been so weak that it would have been overshadowed by the action of the fibers already established.

CONCLUSION

No adaptive functional adjustment of the nervous system took place in these rats after the connections from the spinal

centers to antagonistic limb muscles had been exchanged. The crossing of the peroneal and tibial nerves and the crossing of the pure muscular branches of these nerves resulted in an awkward and thoroughly abnormal foot movement in the former case and in a complete reversal of foot movement in the latter, neither of which was ever corrected by automatic reflex regulation or by a gradual learning or conditioning process. These results are in agreement with those of Cunningham (1898) who crossed the median and ulnar nerves in dogs and stood alone in maintaining that recovery of normal muscular coordination does not follow the crossing of limb nerves. They indicate that the more numerous reports implying a surprising plasticity and regulatory adaptability of the central nervous system to disarrangements of the normal peripheral relations are not to be accepted without question, and show in contrast an extremely unplastic fixation of the basic motor patterns for hind limb coordination.

Persistence of the original patterns of discharge to the limb musculature after peripheral alterations that thoroughly disrupted the normal array of afferent stimuli from the limb supports the contention that the control of limb coordination is in large part central. As pointed out by Gray ('39), peripheral stimuli are extremely important in the timing of limb responses, in controlling the intensity of limb responses, and in determining in many cases which of various possible limb responses as wholes will be set off. But since the elementary patterns of limb coordination persist in the rat after extreme distortion of peripheral conditions produced by nerve crossing, muscle transposition, and even complete deafferentation of the limb; the organization of the intrinsic motor patterns themselves must depend primarily on central rather than peripheral factors.

Permanent retention of the original incidence of discharge of the motor nerve fibers after their regeneration into foreign antagonistic muscles also demonstrates that nerve cells in juvenile and adult stages of the rat are no longer in a sufficiently labile condition to be respecified by foreign muscles.

In amphibians where modulation of nerve by muscle has been most thoroughly studied it has been shown that in larval stages respecification takes place quite readily, while in newly metamorphosed toads it occurs only very slowly (Weiss, '36, p. 516), and in fully grown toads the capacity of nerve cells to undergo modulation is completely lost (Weiss, unpublished). Mammalian tissues in general are less labile than those of amphibians and their nerves probably become irreversibly determined in an earlier stage of development soon after reaching the muscles.

The results in the rat are not necessarily contradictory to the results in larval amphibians in their implications regarding the role of inter-neuron connections in reflex activity and central nervous function. Nerve modulation may be considered an embryological inductive influence which affects development of the central connections of motor cells in the cord rather than a factor which selectively modifies the nerves' sensitivity to central excitatory agents. According to this interpretation, the formation of synaptic terminations on motor cells by the telodendria of internuncial neurons is conditioned by the specific biochemical properties induced in the different motor cells by their muscles. End-organ connection formed by outgrowing nerve fibers in ontogeny becomes, on this basis, an important factor in the laying down and differentiation of central reflex relations. The influence of peripheral organs on the quantitative development of the central nervous system has already been well demonstrated (see Detwiler, '36).

After crossing peripheral nerves, one would expect a restoration of normal function due to modulation of nerve by muscle, according to this interpretation, only in cases where the peripheral nerves had not already become irreversibly determined by their original end-organs and where the central nervous system was still in a sufficiently labile condition to permit compensatory growth readjustments in the central connections and also where the central terminations of the nerves crossed were located in the same region of the central

nervous system. At present there is no crucial evidence to indicate whether modulation affects the selective sensitivity of the motor neurons or the central connections of these neurons. But because this alternative explanation of the phenomenon of homologous response is consistent with both the amphibian and mammalian experiments and also with the classical conceptions of central nervous physiology it is mentioned here as a working hypothesis.

SUMMARY

1. In ten rats (eight unilateral and two bilateral cases, operated at ages ranging from 40 to 250 days) exchanging the nerve connections of flexor and extensor muscles in the shank produced a reversal of foot movement.

2. In all ten cases the foot movement remained fixedly reversed to the end with no corrective modification whatever. Seven cases were kept longer than 15 months after the operation. Immobilization of the contralateral hind foot, training the rats to rise upright on their hind legs for food, and amputation of both front legs at the shoulder all failed to induce reeducation.

3. Post-mortem examination and physiological tests showed that nerve regeneration had been as intended, that sensitivity of the shank and foot had not been impaired by the operation, and that sensory as well as motor fibers had reinnervated the muscles. Severance of the crossed nerves abolished the reversed movement. Control animals, similarly operated except that the nerves were reconnected to the original muscles, showed foot movement in normal phase in all activity.

4. In two additional rats, both unilateral, transposition of flexor and extensor muscles after the nerves to these muscles had previously been crossed resulted in foot movement in normal phase. No change toward reversal occurred after 15 months.

5. In twenty rats, ranging in age from 15 to 80 days, the peroneal and tibial nerves were crossed instead of the single nerve branches to individual muscles. This operation pro-

duced an abnormal limb coordination characterized by indiscriminate contraction of the shank muscles and a predomination of plantar flexion of the foot. This abnormal coordination persisted for 18 months without any sign of a central nervous adjustment.

6. The results furnish new evidence of the rigid organization in the rat of the basic motor patterns for hind limb coordination. They also show that, in a mammal, motor nerve cells in post-embryonic condition do not have the capacity to undergo muscle-specific modulation after regeneration into foreign muscles.

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TRANSPLANTATION OF MOTOR NERVES AND MUSCLES IN THE FORELIMB OF THE RAT

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EIGHT FIGURES

Previous experiments have shown that in the rat a reversal of foot movement results when flexor and extensor muscles of the shank are transposed or when the nerves to these muscles are crossed. This reversal of foot movement, although extremely awkward and in many activities a distinct hindrance to the animals, persists permanently in all activity without any correction of the distorted peripheral effect by central nervous adjustment. Special training, amputation of the contralateral hind food, or amputation of both forelimbs fails to induce reeducation (Sperry, '40, '41).

The present paper deals with similar experiments carried out on the front leg to find out if the central mechanisms for forelimb coordination are any more adaptable to peripheral disarrangements than are those for hind limb coordination. There are several lines of evidence which suggest that readjustments in motor coordination impossible in the hind limb might occur in the forelimb. It has been reported that in man reeducation is effected more readily after transposition of arm muscles than after transposition of leg muscles (Scherb, '38). Histological studies indicate that in rodents there is a richer supply of fibers distributed from the cortex to the forelimb centers of the spinal cord than to the hind limb

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centers. In many lower mammals the cortico-spinal tract does not extend beyond the brachial segments, though in the rat and other rodents it is traceable into the lumbar segments (Kappers, Huber and Crosby, '36). The effects of cortical lesions (Van der Vloet, '06), electrical stimulation of the cortex, and transection of the cortico-spinal tract (Barron, '34 b) in the rat also indicate a greater and more direct influence of cortical activity on forelimb movement than on hind limb movement. In addition front leg movement in the rat shows greater variation than hind leg movement, enters more frequently the visual field, and has more direct effect on the orientation and posture of the animal. Thus conditions in the case of the forelimb would seem to be more favorable than in the hind limb for the dissociation and reorganization of the innate coordination patterns to meet experimental alterations of the motor periphery.

Voluntary control of individual muscles of the arm is possible in man and the contraction phase of any arm muscle, after transposition, can be shifted by training to that of any antagonistic muscle (Scherb, '38). In amphibians, on the contrary, the normal motor coordination patterns of the entire forelimb are unalterable by learning and remain unmodified after peripheral disarrangements that make their persistence more disadvantageous than would be no movement at all (Weiss, '37).

In forms intermediate in the vertebrate scale between man and amphibians the situation is less clear. Flourens (1842) reported recovery of flight in the fowl after crossing the median and ulnar nerves of the wing. Osborne and Kilvington ('10) reported recovery of coordination in the forelimb of the dog after the original median nerve trunk had been substituted by that from the contralateral forelimb. Like Flourens they attributed the recovery to a learning process. According to Kennedy ('14) recovery of coordination occurs immediately after regeneration of crossed flexor and extensor nerve trunks in the forelimb of the dog without any training period and probably is not due to a learning process

but rather to direct modification of central activity by the altered sensory stimuli. By nerve anastomoses Barron ('34 a) forced the median and ulnar trunks of the forelimb to innervate the hind limb in the rat and found that in some cases the resultant associated movements of fore- and hind limbs became gradually dissociated. The dissociation of function in the forelimb centers was attributed to a learning process dependent on a substantial supply of afferent fibers in the crossed nerves. In contrast to the above reports, Cunningham (1898) found no corrective adjustment whatever in the forelimb coordination after crossing the musculospiral with the ulnar and median nerves in the dog. He directly opposed the contention that central nervous mechanisms adjust their impulses through practice to suit an altered peripheral innervation.

Whether the basic central mechanisms for forelimb coordination can be disintegrated and reorganized in the lower mammals and if so, by what means and to what degree, are questions that still remain unsatisfactorily settled in the light of these conflicting reports and interpretations. In all of these previous experiments the nerve sutures were made on large nerve trunks. It is uncertain whether reeducation is possible even in man after the haphazard reestablishment of peripheral connections which results from the random regeneration of complex nerve trunks (Ford and Woodhall, '38; Stookey, '22).

The present experiments were undertaken in the hope that results of a more conclusive nature could be brought to bear on the problem by crossing only terminal nerve branches to specific muscles and by transposing muscles with their nerves intact. The nature of the peripheral derangement produced by these methods can be more exactly determined and controlled. Moreover, these methods produce less extreme shuffling of the original neuron connections between the centers and the periphery. And finally, readjustment is not prevented by the termination of different branches of the same neuron on end organs of different kinds. Control operations were performed

and control cases run throughout with the experimental groups. All but the test muscles acting on the joint in question were excised to prevent readjustment by "trick" movements produced by non-test muscles.

The object of the experiments was to find out if the rat would be able to interchange the timing of the central discharges for elbow flexion and extension in order to restore normal limb coordination after the flexor-extensor relations of the periphery had been reversed by muscle transposition or nerve crossing.

ONE-WAY CROSS: FLEXION REVERSED TO EXTENSION BY MUSCLE TRANSPOSITION

In view of the complete refractoriness to adjustment exhibited by the rat after experimental reversal of hind foot movement shown in the previous experiments, an attempt was made in the first series of operations to establish the simplest and most favorable conditions for reeducation. In these cases only flexor muscles of the elbow were transposed, no extensors, so that readjustment of flexor action only was necessary. Possible reflex inhibition of learning by proprioceptive stimuli from antagonistic muscles, as reported in human patients (Scherb, '38), was excluded by removal of all the extensor muscles of the joint. To make unnecessary a dissociation of function within the agonist group of elbow flexors itself, the other flexor muscles which were not transposed were also removed. Thus all that was required for adjustment was a chronological shift in the functional relations between the brachial flexors and the musculature of the other limb segments.

The operation

The tendons of the biceps and brachialis muscles were cut from their insertions and sutured to the distal stump of the severed tendon of the long head of the triceps muscle (fig. 1) so that these two flexor muscles were made to act as extensors.

All other brachial muscles including the anconeus and pronator teres muscles were excised, leaving only the two crossed flexor muscles acting on the elbow joint. It was necessary in most cases to cut the cutaneous branch of the circumflex nerve to the skin over the shoulder; all other nerve branches save those to the excised muscles were left intact. All shoulder

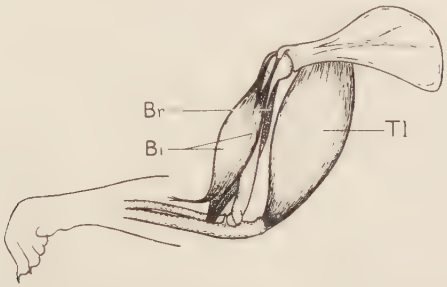

Fig. 1 Diagram of the test muscles in their normal anatomical positions. Br, M. brachialis; Bi, M. biceps brachii, caput longum and caput breve; Tl, M. triceps longus.

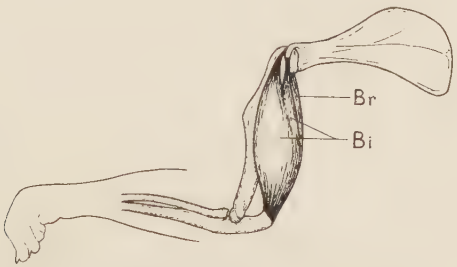

Fig. 2 Diagram of flexor muscles of the elbow (M. biceps, Bi; M. brachialis, Br) after being transposed to act as extensors.

muscles were left in place except the small coracobrachialis muscle which was removed to make more room for the crossed biceps muscle. The diagram in figure 2 illustrates the resultant anatomical relationship of the flexor muscles after transposition. Two control rats were prepared also in which all the brachial muscles acting on the elbow joint were excised except the long triceps [2] extensor which was left intact. The

[2] For the sake of brevity, the long head of the triceps and long head of the biceps will be referred to as the long triceps and long biceps respectively.

operations were performed under a combination of ether and sodium amytal anesthesia with a single lateral incision. The tendons were sutured with fine silk thread.

Results

Active elbow extension began to appear at varying periods from 7 to 19 days after the operation, recovery being quicker in the younger animals. The extensor movements occurred from the beginning in reverse phase. The elbow was sharply extended in the suspended flexor phase of locomotion instead of in the supporting extensor phase. In the flexion or withdrawal reflex the elbow was extended strongly; whereas it remained limp or was extended only weakly in the controls. In landing on the front legs, the forearm, instead of extending to support the body weight as in controls, remained loose and was flexed passively so that the animal's weight fell on the elbow. In reaching to free a binding placed about the neck, an action involving elbow flexion in the normal animal, the elbow was stiffened out in extreme extension so that the paw reached far beyond the binding. When the rats were suddenly rotated toward the side of the operated limb, the limb remained limp instead of extending against the floor to counteract the rotation as it did in normal and control animals.

Fifteen successfully operated cases were obtained which showed this extension of the elbow in movements normally involving elbow flexion, and a looseness of the elbow joint in movements normally involving elbow extension. Extension of the elbow by the crossed flexor muscles and passive flexion by the body weight prevented ankylosis of the joint. The fifteen cases with the transposed flexor muscles ranged in age from 20 days to 60 days at the time of operation. These cases were kept under observation and tested to see if they could learn to support themselves on the operated limb by using the transposed flexor muscles to extend the elbow.

The first three rats successfully operated upon continued to move the elbow in reverse for several weeks, meantime relying on the unoperated limbs for support during locomotion

and other activity. It therefore became necessary to make the use of the operated limb in unreversed fashion more crucial to the animals. This was accomplished effectively by amputating the contralateral forelimb, the ipsilateral foot, and the tail which the rats used considerably for balance and support. The absence of the contralateral limb also made it possible to determine more reliably just how much the animals were actually depending upon the operated limb. All cases, therefore, were treated uniformly in this manner thereafter as soon as the transposed muscles had begun to function. In this condition, the only way in which the animals could raise their forequarters off the floor while moving about was by use of the operated forelimb. They were thus in a state of training whenever they moved. Moreover, these extreme measures served another important purpose in that they tended to break up the normal automatic patterns of coordination and bring out new, more voluntary activity. Such conditions have been shown to favor reeducation after muscle transposition in man (Scherb, '38).

After this treatment all but one of the rats managed to support themselves to some degree on the operated front leg with the elbow extended. They accomplished this, however, by a trick method quite different from that used by normal rats. Reversed action of the transposed flexors frequently brought the elbow joint into a locked position in extreme extension. Once the joint became thus fixed, it was used in the mechanically stabilized position aided by an inward rotation at the shoulder to support the forebody. In locomotion the limb was moved from the shoulder in a stiffly extended locked position. It was swung forward out at the side and then used for support much like a crutch. Whenever the joint slipped out of the locked position, the limb caved in and the rat came down on its elbow. The one case which never showed this trick adjustment was found to have a partial ankylosis which prevented extreme extension and locking of the joint. The controls never displayed the characteristic locked joint method of supporting themselves shown by the

experimentals. Like normal rats, they raised and upheld the forequarters with the elbow joint maintained in varying degrees of extension.

The elbow joint of the rat does not lock completely by extending beyond 180 degrees as does the elbow in many human beings. When the forelimb is fully extended in the supporting position, however, it is capable of upholding a weight several times the body weight of the rat. The downward pressure is taken up almost entirely by the mechanical structure of the bones and ligaments with only a slight and relatively insignificant amount of active muscular work being required to hold the joint in the mechanically stabilized position. The use of the forelimb in this manner so that the body was supported primarily by the mechanical features of the elbow joint, rather than by muscular work at the joint, is referred to here as a locked joint reaction.

No training period was observed in the onset of the trick locked joint reaction. It appeared abruptly on amputation of the other limbs. In most of the cases it appeared for the first time as soon as the animals began to move on coming out of the anesthesia after the amputations. As the animals' excitability subsided and they became more relaxed, there was a certain amount of relapse back to discrete reversed action. In the early stages thereafter when the limb went into the locked position, it was held out sidewise from the body and only occasionally, apparently by accident, was the body weight shifted directly on top of the extended limb. As time went on, however, the effective use of the locked limb in a supporting position became less accidental and more consistent and somewhat more proficient. This gradual though slight improvement in the use of the locked joint reaction for support after it had once appeared apparently involved a training process.

The initial appearance of the locked joint reaction was not completely dependent on the amputations. In a few of the cases the reaction appeared before the amputations were made. In these cases, however, very little of the body weight

was shifted onto the operated limb. The reaction could be readily elicited in cases which had only the contralateral forelimb amputated and which had not yet shown it spontaneously, by holding the rat up by the hind quarters and pushing it slowly along the floor on its forebody. The amputations merely favored the appearance of the reaction and made its retention and improvement thereafter more necessary to the animals.

There was considerable range in the degree of success with which the various cases used the operated limb to support themselves. In some cases elbow extension remained in reverse most of the time, and it was only exceptionally that the animals happened to raise their forequarters off the elbow and lean on the straightened locked forelimb. This occurred most frequently while they were pivoting about on the hind quarters and only rarely during locomotion. At the other extreme were cases that came to use the extended limb for support with considerable certainty and in which it was only on occasional instances that the joint gave way under them. One of these cases after 9 months is pictured in figure 3 supporting itself on the operated limb while stretching for food. At times these rats were able to maintain their support in the position shown in figure 3 during extreme and rapid shifts of head, neck, and trunk posture.

When the joint slipped out of the locked position, the animals usually fell from the platform. But two of the rats were observed to avoid falling sometimes by quick extension of the elbow before the joint had become more than slightly flexed. Except for these corrective movements that appeared in the advanced stages of the two most proficient cases, the act of extending the joint to the locked position was always performed in the reverse phase of coordination, that is, in the normal flexor phase of limb movement when the body weight was being shifted off the limb, not onto it. Even in the case of these corrective movements it is probable that although the weight of the forequarters was falling onto the operated limb, the muscular contractions of the back and hind legs were of a nature to counteract this fall and were thus similar

to those involved in shifting weight off the forelimb, rather than onto it.

In any case, the act of getting the limb into the beneficial locked position in most instances demanded no adjustment in the function of the transposed muscles. It was only the ability to maintain this position during the supporting phases of activity that involved a corrective modification of the reversed

Fig. 3 Rat with transposed flexor muscles feeding from training platform. The training apparatus was so constructed that the rats, in order to reach food contained in the self-feeder at upper left, had to climb stairs to platform, span distance to prop, and then support forebody on the operated limb as shown in picture. Photograph illustrates most proficient case of the series. Even this animal usually fell to floor 22 cm. below when the elbow joint slipped out of the locked position (see text).

movement of the elbow. There was some tendency, though not very marked, for the cases operated young to show greater proficiency than the old ones.

Cutting the nerves to the transposed muscles in one case and the tendons of the transposed muscles in another case abolished the reversed action of the elbow and the locked joint adjustment. In another case the nerves to the transposed muscles were merely crushed. Both the adjusted and the reversed action of the elbow disappeared and reappeared

after 4 weeks when the nerves had regenerated. Clearly the reversed extension of the elbow was produced by contraction of the transposed muscles and this contraction was necessary to bring the joint into the locked position where it could be used for support.

Four additional experimental cases were prepared similarly to the others except that in two of them the biceps muscle was excised and only the brachialis muscle crossed, while in the other two the brachialis was excised and only the biceps crossed. All four cases showed the typical locked joint adjustment, while all actual movement of the elbow remained reversed. Since it appeared after crossing either muscle alone, the trick adjustment was not linked up with the two-joint action of the biceps muscle nor with any reaction peculiar to either one of the muscles.

The cutaneous nerve to the skin over the shoulder regenerated in all cases. No loss in sensitivity over the rest of the limb was detected. The elbow and shoulder joints remained normally loose and flexible. Function of the forearm and paw muscles was unimpaired. The wrist was extended and flexed in normal phase while the elbow moved in reverse. The digits were extended in the landing reaction and grasped tightly the wires of the cage when the animals were lifted out.

Two additional controls were prepared like the other controls except that the large triceps muscle was sheared down to a size no larger than the combined size of the biceps and brachialis muscles. These cases never resorted to locking the elbow joint for support, but maintained themselves with the joint in various degrees of extension with tension on the reduced triceps muscle. The same was true of two other controls in which all brachial muscles were excised except the small medial triceps. This muscle is smaller in size than the combined size of the flexor muscles, and its mechanical relations are quite similar to those of the transposed flexor muscles.

The experimental cases when examined under anesthesia showed no atrophy of the transposed muscles (note transposed flexors in fig. 7). On the contrary a slight hypertrophy was

apparent in many of the cases. The length of the muscles was nicely adjusted. The anatomical conditions for this transposition at the elbow are very favorable. That the operated limb was capable of strong and vigorous elbow extension was also evident from struggling movements made during manipulation. That the transposed muscles were strong enough to lift the full weight of the forebody was shown by the fact that they did so during random struggling movements when the rats were held by their hindquarters with the forebody resting on the floor. The use of the joint in the locked position for support instead of in the normally somewhat flexed position, cannot be ascribed, therefore, to weakness of the transposed muscles.

Ten of the experimental cases were kept longer than a year. The four cases showing greatest adjustment were kept for 16 months. In all cases the withdrawal reflex remained in reverse to the end. When the palmar surface of the paw was pricked with a needle from behind, the paw, instead of being withdrawn, was driven harder against the needle by extension of the elbow. All cases continued permanently to extend the arm sharply in trying to locate points about the face or in trying to brush off a binding placed about the neck. When the operated limb was lifted over obstacles or over steps in climbing up stairs, the transposed muscles continued to work in reverse so that the limb was stiffly extended and had to be raised upward far out to the side in order to clear the steps and other obstacles. In the controls the elbow remained loose in these reactions in a neutral position of half flexion which was more advantageous than the stiffly extended position. In order to get to the platform shown in figure 3 the rats had to climb up stairs. To get down they usually jumped to the floor from the platform or from halfway down the stairs rather than descend the stairs, which was difficult for them. None of the cases ever learned to break the fall in landing by contraction of the transposed muscles. The muscles relaxed so that the limb caved in and the animal's weight fell on the elbow. Like normal rats the controls landed on

the forepaw, not on the elbow. Use of the limb in the extended, locked position for support was thus the only reaction which seemed to involve any adaptive alteration in elbow movement.

To determine whether maintenance of the joint in the locked position during the supporting phases of movement involved any muscular contraction or was dependent entirely on the mechanical relations of the joint and ligaments, the following operation was performed (fig. 4). A small hole was drilled in the humerus at the point where the olecranon process of the ulna closes against it in extreme extension. A small peg made from a metatarsal bone was inserted firmly into the hole

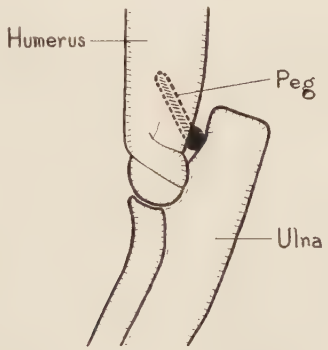

Fig. 4 Diagram illustrating how peg inserted into humerus prevented elbow joint from locking.

in the humerus so that only the epiphysis of the metatarsal peg protruded. This was filed down until it was just long enough to prevent the elbow joint from locking. The joint could thus be extended approximately 170 degrees but could not be brought into complete extension. This operation was performed on one of the cases that had been using the operated limb consistently for support for more than 10 months and had learned to feed from the training platform as shown in figure 3. The forelimb was rendered practically useless as a means of support by the pegging operation. Whenever any appreciable weight was put on the forelimb, it caved in at the elbow. The rat was no longer able to support itself on the

training platform so as to obtain food when tested 2 weeks after the peg was inserted. On some occasions, however, during rapid locomotion and especially when the animal was at rest with most of its weight on the hind quarters, extension of the elbow was maintained during the supporting phase of coordination. A certain amount of weak muscular tension was apparently present at this time. The muscular tension involved in the trick adjustment shown by all but one of the rats in this series was too weak evidently to furnish any appreciable support itself, even after 10 months of practice, but was sufficient to maintain the joint in the locked position so long as most of the body weight was taken up by the non-muscular, mechanical structures.

Contraction of the shoulder muscles as well as of the test muscles could have produced the slight tension required to hold the joint in the locked position during the supporting phases of movement. Adduction of the forelimb accompanied by an inward rotation of the humerus would necessarily produce also a secondary extensor action at the elbow joint when the fore foot was fixed against the floor. That it was actually the shoulder muscles and not the test muscles that were primarily responsible for maintaining the joint in the locked position during the supporting phases of movement was shown by the following: Cutting the tendons of the latissimus dorsi and pectoral muscles on two cases 12 months after operation completely abolished the trick adjustment. On the other hand, severing the tendons of the spinodeltoid, acromiodeltoid, and infraspinatus muscles on two other cases produced no deleterious effect on the locked joint adjustment. Normal and control animals were able to support themselves on the forelimb in locomotion and other activity with little noticeable deficiency after severance of the tendons of either the above adductor or abductor group of shoulder muscles.

Whether the transposed flexor muscles were aiding the shoulder muscles to some slight degree to keep the joint locked could not be determined by observation alone and, hence, action potential recordings were made. Two fine enameled

silver wires, one for the active lead and one for ground, were cemented together side by side. The two cut ends of the wires almost in contact served as the electrodes. These electrodes were fastened under the skin just over the muscle or in some cases directly under the perimysium of the test muscles. Records were taken from the three cases which after 14 months showed the greatest proficiency in supporting themselves on the operated limb. The action potentials, amplified and recorded through a loudspeaker and oscillograph, were correlated with the rats' limb movements.

During locomotion, when the forelimb was kept rigidly extended, the contraction of the transposed flexors was distinctly intermittent, instead of being sustained throughout the locomotor cycle. The bursts of contraction occurred, moreover, not during the supporting phase of walking to help maintain elbow extension but during the suspended flexion phase of walking as in normal animals. That this was the exact phase of contraction was further substantiated by synchronized motion picture and oscillograph records [3] (fig. 8). The slight muscular tension required to maintain the limb in the mechanically stabilized position of complete extension during the supporting phase was evidently furnished entirely by the intact adductor muscles of the shoulder and not at all by the transposed muscles. The transposed muscles after 14 months of practice were, therefore, still working in their original locomotor phase in spite of the fact that action in just the opposite phase would have been much more to the animals' advantage for either this stifflegged type of walking or normal walking.

At times when the rats were at rest supporting the forebody on the locked limb, there occurred a certain amount of weak discharge in the transposed muscles. This weak discharge, however, could not be distinguished from flexor discharge in normal animals under similar conditions. Regarding the action of the transposed muscles in other responses, the

[3] The synchronized action potential and motion picture records were taken with the aid of Paul F. Brown.

action potential records merely substantiated the previous conclusions based on observation of elbow movement, namely, persistence of the original time pattern of activation of the transposed muscles.

ONE-WAY CROSS: FLEXION REVERSED TO EXTENSION BY CROSSING NERVES

In the rat, unlike the situation in amphibians, there is no evidence that normal coordination is restored through modulation of nerve by muscle after nerves are crossed to foreign muscles. The discoordination produced by crossing nerves is similar to that produced by transposing muscles and can be used in the same way to test the modifiability of central mechanisms by experience and training (Sperry, '41). In the present experiments the normal timing of elbow extension was reversed by crossing the nerve of the biceps flexor into an extensor muscle, the long triceps.

The operation

The nerves to the biceps muscle and the long triceps muscle were severed, and the proximal stump of the biceps nerve was crossed to the distal stump of the triceps nerve. To prevent regeneration of the triceps nerve into its original muscle, the proximal stump was ligated tightly with silk thread and inserted into tissue as far distant as possible from the triceps muscle. To expose the nerves better, the tendons of the deltoid and pectoral muscles were partially severed from the humerus. The biceps and coracobrachialis muscles were excised and a section of the nerve to the brachialis muscle was removed where it crossed the humerus. The brachialis was thus paralysed to give the weakened extensors a better chance to extend the elbow completely and so prevent possible ankylosis of the joint during the period in which the crossed nerve was regenerating. The nerve crosses were tubulated in arterial sheaths as described by Weiss ('41 a). In a few cases the brachialis nerve as well as the biceps nerve was crossed to the triceps muscle but no detectable difference ap-

peared in the results. The operations were done through a medial incision in the axilla. About a month and a half later when the flexor nerve had regenerated into the triceps muscle, the other brachial muscles including the brachialis, anconeus, and pronator teres were excised through a lateral incision. This left only the long head of the triceps muscle supplied by the biceps nerve to effect elbow movement as shown in figure 5. After the operated limb had healed, amputations were performed as in the muscle-cross group. In two control

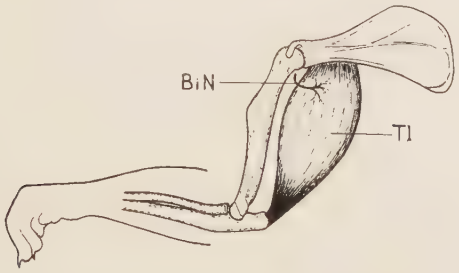

Fig. 5 Diagram illustrating anatomical situation after innervating the long triceps extensor (Tl) by the nerve (BiN) of the biceps flexor.

cases all brachial muscles acting on the elbow were removed except the long triceps which was left in its normal position with its nerve intact. The tendons of the pectoral and deltoid muscles were partially severed as in the experimental cases.

Results

Seven experimental cases were obtained which showed good elbow extension in reversed phase. Three of these cases were 15 days, the others ranged up to 30 days in age at the time the nerves were crossed. No reliable age difference was noted in the results. These animals were kept under observation from 4 to 15 months. When sacrificed they were carefully dissected and tested for misregeneration of nerve fibers. Electrical and mechanical stimulation of the cut end of the biceps nerve above the point of suture produced sharp strong contraction of the triceps muscle. No contraction occurred in

this muscle when the trunk of the original triceps nerve was cut and stimulated. There was no sign of misregeneration in any of these seven cases. The triceps muscle after reinnervation by the biceps nerve was in no case reduced by more than one-seventh normal size, showing that a few nerve fibers from a small muscle are capable of reinnervating a much larger muscle by multiple axon branching. At postmortem dissections the nerve to the triceps muscle was found to be distinctly larger, by approximately one-third, distal to the region of anastomosis than proximal to it.

Anatomically these cases were quite comparable to the control cases, the only difference being that in the experimental group the triceps was supplied by the biceps nerve instead of its original nerve. Forelimb function in the experimental cases, however, was not at all comparable to that in the controls. Briefly its history was quite similar to that previously described for the cases in which the flexor muscles were transposed. These cases displayed the same type of reversed movement and the same kind of trick adjustment. In two cases the elbow moved in reverse most of the time and was used for support in the locked position only rarely. In other cases the adjustment was fairly good and the animals supported themselves much of the time on the stiffened, unnaturally extended limb. Those showing the greatest adjustment never became quite as proficient as did some of the animals in the preceding muscle-cross series. This may be attributed to the partial severance of the tendons of the shoulder adductor muscles during the operation when it was not foreseen that these muscles would be of such importance in postoperative adjustment. No compensating adjustment for this deficiency in the shoulder muscles ever appeared in the action of the test muscles in these cases. As in the muscle-cross cases the trick method of mechanical support constituted the only adjustment observed in elbow movements.

Since the same type of adjustment that followed muscle transposition occurred also in these rats in which the muscle attachments remained normal and only the nerves were

crossed, its nature must not have been due in the muscle-cross series to any peculiarity of the unnatural mechanical conditions of the transplanted muscles.

It is important to note that this locked joint adjustment that occurred naturally in both series of cases furnished a better condition for testing the rats' learning ability than any training situation that could have been devised experimentally. In itself, it was a direct approach to the important first step of re-education, namely, the production of a favorable trial reaction which could be selected for and improved upon, while the unfavorable reversed movements were eliminated. Had the animals been capable, under any conditions, of correcting the innate action phase of the flexor motor neurons, one would expect them to have done so from this excellent point of departure by gradually improving upon the awkward unstable locked joint support until a more effective normal use of the elbow was restored.

As in the preceding series, the trick adjustment in these nerve-cross cases was followed carefully and tested for any signs of improvement that might indicate a corrective shift in the timing of the test muscles. In one of those cases which showed the greatest degree of adjustment and which had been using the operated limb for support for nearly 9 months, a bone peg was inserted in the humerus as illustrated in figure 4. After the operation the elbow joint was extended to about 170 degrees but could not be extended completely. As a result the rat was unable thereafter to support itself on the extended forelimb. The trick adjustment was likewise abolished by severing the tendons of the shoulder adductor muscles in a third case. Action potential records taken on two other cases 13 months after the primary operation showed that the triceps extensor supplied by the biceps nerve was still contracting in the uncorrected flexor phase of locomotion and other activities. Thus, as in the muscle-cross series, these various checks showed that the rats, even after 9 months and more of practice, had acquired no discriminate control over the flexor motor neurons during the extension phase of co-ordination.

The fact that the one peculiar type of adjustment reaction and no other type appeared consistently in so many cases, and the fact that its onset was abrupt without any training period, both indicated that the underlying pattern of muscular contraction involved was not one that was entirely novel to the action system of the rat, but rather a motor pattern normally present in the rat's repertoire of reactions which happened to work beneficially under the conditions of the experimental disarrangement. Action potential analysis and the results of severing the tendons of the shoulder muscles confirmed this conclusion and showed that the adjustment was achieved by the action of the intact shoulder musculature and not by a corrective shift in the timing of the test muscles. The gradual, but not very marked improvement in the proficiency with which the rats used the locked limb for support must be ascribed entirely to improvement in the action of the adductor muscles of the shoulder and to improvement in the general ability to balance on the straightened limb without throwing it out of the locked position.

The trick adjustment was in no sense a restoration of normal coordination, nor was it at all the best adjustment that might conceivably have been made in the centers to suit the altered peripheral conditions. The normal elbow extension of the controls was decidedly more beneficial to the animals in all activities than was the reversed movement and awkward unreliable stiff-legged support used by the experimental cases.

SPLIT CROSS: ONE FLEXOR MUSCLE TRANSPOSED FOR EXTENSION, ANOTHER LEFT IN NORMAL POSITION FOR FLEXION

In these cases the action of the group of elbow flexors was split by transposing one flexor muscle to act as an extensor against another flexor left in normal position. This type of operation in which a muscle is transplanted to act against its own original group of agonists is performed commonly on human patients. It requires for restoration of normal coordination a dissociation and reorganization of the functional relations not only between muscles of different

limb segments, but also between muscles belonging to the same agonist group within a single limb segment.

The operation

Through a medial incision in the axilla the nerve to the long biceps was crushed and the short head of the biceps muscle and coracobrachialis muscle were excised. Two or 3 days later the brachialis muscle was transposed and the remaining brachial muscles except the long biceps and the small pronator teres muscle were removed entire as in previous operations. The nerve to the biceps was crushed, thus temporarily paralysing the muscle, in order to prevent it

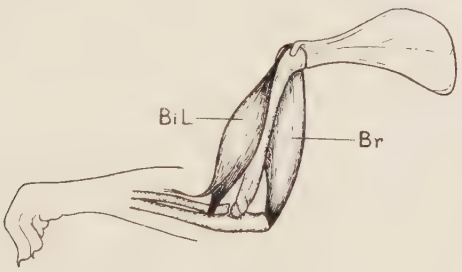

Fig. 6 Diagram showing long biceps (BiL) left in normal position and brachialis flexor (Br) transposed to act as an extensor in antagonism to its former co-flexor, the biceps.

from pulling loose the newly sutured tendon of the brachialis muscle. Nine cases, all between 20 and 30 days of age, were so operated. The anatomical effect of the operation is diagrammed in figure 6. The pronator teres muscle, the flexor action of which proved to be so weak as to be easily overpowered by the transposed brachialis muscle, did not figure in the results and is omitted for the sake of clarity in the figure. The experimental cases were compared with controls in which all brachial muscles were excised except the long biceps and long triceps, and also with the two experimental cases in the first series in which only the brachialis muscle was transposed.

Results

Four of the cases began to show active elbow extension in reverse within a week after the muscles were transposed. This reversed extension disappeared, however, in a few days when the biceps muscle began to recover function. The biceps, contracting at the same time as the mechanically antagonistic brachialis, easily overpowered the newly transposed muscle. By the tenth day the biceps muscle in all nine cases had recovered function and was overpowering the brachialis muscle so that extension of the elbow no longer occurred in any of the animals. Either the biceps nerves had regenerated very rapidly or had not been completely crushed. Two of the rats that had previously shown elbow extension in reverse were allowed to continue without further operation except that the unoperated limbs and tail were amputated as in the previous series. The flexor action of the biceps continued to predominate permanently over the extensor action of the brachialis in these animals. They never managed to dissociate the action of the brachialis muscle from that of the biceps so as to extend the elbow joint during the relaxed phase of the biceps. Nor did they learn to inhibit the action of the biceps so as to extend the elbow in reverse phase and bring it into the locked position.

In the other seven animals the nerve to the biceps was crushed again on the tenth day so thoroughly that in some cases it was severed completely. Five days later all seven rats displayed active extension of the elbow in reverse phase. Their contralateral forelimb, ipsilateral foot, and tail were then amputated as in the other cases. In one animal the biceps began to function again within a week and extension of the elbow was permanently prevented thereafter by the predominance of flexion.

It was 5 weeks after the second crushing of the nerve before there was any sign of biceps recovery in the other six animals. In the meantime all six of these rats had come to use the operated limb in the typical locked joint manner

[illegible] for supporting the forearm in locomotion and other activities with varying degrees of proficiency. During the fifth and sixth weeks a partial loss in the ability to use the operated limb for support was apparent in three of the cases. After 6 weeks two of the animals were no longer able to maintain extension of the elbow during the supporting phases of movement. One of these two cases 5 weeks earlier had been the most proficient of the group in supporting itself on the operated forelimb. Of the other pair, one had lost the ability to support itself during locomotion but managed to do so unnecessarily while at rest. The remaining three still used the operated limb for support without any noticeable impairment.

The three animals that showed no impairment of the locked limb adjustment were examined under anesthesia 9 weeks after the biceps nerve had been resutured. The nerve had regenerated and the biceps muscle was full-size and looked perfectly healthy in all three cases. When the biceps nerve was stimulated electrically, the muscle contracted strongly as indicated by change in shape but produced only a small degree of flexion of the elbow instead of the vigorous complete flexion produced by similar stimulation of the biceps nerve in normal animals. Evidently the persistent stretching of the biceps by the transposed brachialis during the period of paralysis had increased the resting length of the biceps muscle. Thus the muscle, although being activated in these cases, was too long for its contraction to have sufficient mechanical effect on the joint to counteract the action of the brachialis muscle. This interpretation received further support from action potential records which showed that during [illegible] walking in these cases the biceps was clearly discharging regularly in its original flexor phase in synchronism with the transposed brachialis muscle.

In none of the nine experimental cases was there any sign of innervation of function between the two flexor muscles, the biceps and the brachialis. Although made to act as antagonists mechanically, the muscles continued to contract synchronously.

Depending upon the strength of the muscle and mechanical relations with the joint, one or the other muscle came to overpower the other in different cases so that the joint was either predominantly flexed or predominantly extended but was never flexed and extended reciprocally in the same animal. Even after the brachialis muscle had been used successfully for 6 weeks in two cases to bring the limb into the locked position, the biceps, on complete recovery of function, automatically counteracted the beneficial action of the brachialis muscle so that the rats thereafter were forced to crawl about on the elbow.

TWO-WAY CROSS: FLEXION REVERSED TO EXTENSION AND EXTENSION REVERSED TO FLEXION

In order to support themselves with an extensor as well as flexors acting in reverse, the rats would have to inhibit the action of the transposed extensor during the supporting phases of movement as well as maintain tension in the adductor muscles of the shoulder. These operations were designed to find out if the animals would be able to inhibit the action of the transposed extensor in this fashion and whether they could in addition adaptively modify its positive contraction phase.

The operation

In this series the operation was similar to that in which only the flexor muscles were transposed except that, instead of being excised, the long triceps was transposed to the flexor position. To do this, both the origin and insertion of the muscle had to be transplanted. The broad tendon of origin was sutured with silk thread to fascia and tendons about the anterior head of the humerus. The tendon of insertion was fastened to the medial surface of the ulna at the location of the distal stump of the severed brachialis tendon. Silk thread woven through the insertion tendon was looped underneath the ulna and tied to fascia on the dorsolateral face of the forearm. To make space for the transposed triceps muscle

it was necessary to excise the bulk of the deltoid muscle of the shoulder and to remove part of the deltoid ridge of the humerus. Because the long triceps is very large it was sheared down to about two-thirds normal size. The anatomical effect of the operation is illustrated in figure 7 by photographs of the operated limb of one case dissected 13 months after the operation. The muscles were transposed in this manner on

Fig. 7 Medial (top) and lateral (bottom) views of limb with biceps and brachialis flexors transposed to act as extensors and long triceps extensor transposed to act as a flexor. Tl, M. triceps longus; Bi, M. biceps; Br, M. brachialis. Dissection made at time of sacrifice 13 months after operation. Shoulder and forearm muscles partially removed to expose tendons of test muscles. This is an average specimen. The muscles are somewhat shrunken after preservation for 3 months in formalin.

fourteen rats ranging in age from 22 to 48 days at the time of operation. The contralateral forelimb, the ipsilateral foot, and tail were amputated on all cases within 4 weeks after the operation. Three control rats were prepared in addition in which the operation was similar except that the brachialis muscle was excised and the biceps and long triceps muscles were left in normal position, uncrossed.

Results

Six weeks after the operation five of the fourteen animals showed active extension and flexion of the elbow. These elbow movements were always in reverse phase from that shown in control and normal rats. The elbow was extended in the suspended phase of walking and flexed in the supporting phase. In the withdrawal reflex the elbow was extended. It was flexed when the rats, in falling, landed on the forelimbs. When the rats reached upward toward regions about the ears and neck, the elbow was extended instead of flexed. When the animals were suddenly rotated onto the side of the operated limb, the elbow was flexed instead of extended. When they leaned on the operated limb while at rest, the elbow was flexed. In climbing and lifting movements, the elbow was always extended in the phase in which it was flexed in normal and control rats. Contraction of the transposed flexors in these reactions regularly produced complete extension of the elbow, but triceps contraction produced only about three-fourths complete flexion. Electrical stimulation of the triceps under anesthesia showed that the transposed muscle was incapable of producing as complete flexion of the elbow as does the normal biceps muscle.

All five of these cases were kept under observation for longer than 12 months. In all cases the elbow movements remained permanently in reverse. At the end the elbow movements in some of the test reactions were not so vigorous as at first. Apparently the rats had learned that the operated limb was of little use and tended to inhibit its action. When surprised or excited by rough handling, however, they moved the limb with the former intensity with reverse action at the elbow. None of them learned to support itself on the extended forelimb either while at rest or during locomotion. An attempt was made to train three of them to feed as in figure 3. The self-feeder was lowered time after time to within reach and then raised gradually day by day until it was so high that it could be reached only by using the extended forelimb for

support. The controls had no difficulty in supporting themselves on the extended forelimb while feeding from the training platform. When no learning appeared in the experimental cases after 3 months, the self-feeder was left at a height such that the rats could just barely reach the food with difficulty when the limb was flexed. After 3 weeks more they still showed no sign of learning to extend the limb so as to raise the forebody to a position from which they could get at the food more easily, and this training was discontinued. The limb coordination in climbing the stairs to the platform and in landing on descent was also carefully watched during this period, but no adjustment in the action of the transposed muscles was observed.

Of the other nine rats, two showed active elbow extension which remained in reverse without adjustment. Active overt elbow flexion, however, was absent or at least so weak that it could not be distinguished from passive flexion of the joint. When the triceps muscle was stimulated electrically in these two cases, its contraction flexed the elbow only about 80 degrees, not as much as in the preceding five animals.

The forelimb coordination in the remaining seven rats was quite similar to that in the animals described previously in which only the flexor muscles were transposed. Within 5 weeks after the operation they all managed with varying efficiency to support themselves on the forelimb with the elbow joint in the locked position. There was no indication in any of these cases of active flexion of the elbow. When these rats were examined under anesthesia, it was found that in three cases the insertion of the triceps muscle had been pulled loose so that the muscle had no action on the elbow joint. In the other four animals the insertion and origin were both intact. In one of the four, the muscle was so lengthened that its contraction had no effect on the ulna. In the other three cases electrical stimulation of the triceps caused partial flexion of the joint by not more than 80 degrees.

These three animals in which the triceps on electrical stimulation was found to be capable of exerting an appreciable

flexor action on the joint were kept for 16 months after the muscles were transposed. Active flexion of the elbow, if present in their behavior, remained extremely weak and could not be distinguished from passive flexion. All three continued to use the forelimb in the locked position to support the forequarters. Action potential records were taken in the sixteenth month after the operation. It was found that the transposed flexors were working just as in the one-way cross series, namely, in the original flexor phase of coordination without any corrective shift in timing. The triceps was discharging in the normal unadjusted triceps phase in most of the test reactions. When the animals were successful, however, in supporting themselves on the locked elbow joint, when walking, pivoting about on the hind quarters, or at rest, the triceps muscle did not contract during the supporting reaction as it did in controls. But on those occasions when the same animals were unsuccessful and the joint caved in during these activities, the triceps contracted as it would have had the muscle not been transposed. In locomotion when the locked joint adjustment was not used, the triceps discharged regularly in the supporting phase of the walking cycle. The locked joint adjustment, therefore, involved an alteration in the action of the triceps muscle in that there was an inhibition of its normal contraction phase during the supporting phases of activity. There was no positive adjustment, however, in the timing of its contraction.

The ability of these rats to support themselves on the straightly extended forelimb was dependent on the action of the shoulder muscles as in the previous series. The trick adjustment disappeared in two of the cases upon severance of the tendons of the muscles causing adduction and inward rotation of the humerus, but persisted in the third case after cutting the tendons of the muscles which cause abduction and outward rotation of the humerus.

That the transposed triceps produced an overt flexion of the elbow joint in only five out of fourteen cases while the transposed flexors completely and vigorously extended the

elbow in all fourteen cases can be attributed to the following factors. First, the origin as well as the insertion of the triceps was transplanted and neither of these could be as neatly and firmly sutured as could the tendons of the transposed flexors. Secondly, extensors are inhibited and flexors predominantly contracted in a newly operated or injured limb, a reaction which, under normal conditions, protects the limb. Contraction of the flexors in these animals and the resultant stretching of the passive triceps especially while its tendons were still regenerating would tend to make it recover finally with an abnormally long resting length. Thirdly, as soon as the flexors had recovered sufficiently so that the locked joint adjustment was used, the action of the triceps was further inhibited. These factors plus a better anatomical and mechanical adjustment to the joint all tended to favor the transposed flexors.

Pronounced action of the transposed triceps to produce overt flexion of the elbow was correlated with the absence of the trick adjustment in this series. Whether the locked joint reaction was prevented from the beginning by the early recovery of triceps function or whether the absence of the reaction permitted better recovery and function of the triceps is not certain. Both factors would tend to reinforce each other. Excision of the long triceps after 14 months in two cases which showed overt elbow flexion and no locked joint adjustment was not followed by an emergence of the trick adjustment. The lack of adjustment may have been correlated primarily with the effects on the shoulder muscles of removal of the deltoid ridge of the humerus in the original operation. Postmortem examination of the shoulder musculature, however, did not reveal differences significant enough to bear out this latter interpretation with certainty.

TWO-WAY CROSS: FLEXION REVERSED BY MUSCLE TRANSPOSITION, EXTENSION BY NERVE CROSSING

This series was similar to the preceding except that the difficulties and complications introduced by crossing the triceps muscle were avoided by crossing the triceps nerve into a flexor muscle.

The operation

Through an incision in the axilla the coracobrachialis muscle and the short head of the biceps muscle were excised. The proximal stump of the long triceps nerve was anastomosed to the distal stump of the long biceps nerve with an arterial sheath. The proximal stump of the biceps nerve was ligated and inserted into tissue as far distant as possible from the biceps muscle. Ten days later through a lateral incision, the brachialis muscle was transposed to the extensor position and the remaining brachial muscles except the long biceps were removed. The resultant anatomical condition is similar to that shown in figure 6 except that the biceps muscle was innervated by the nerve of the long triceps instead of its original nerve. Ten animals were operated upon. They were 24 and 25 days of age when the nerves were crossed. The controls in this series were the same as those in the preceding series.

Results

About 7 days after the brachialis muscle was transposed, it began to recover function extending the elbow in reverse. These movements became stronger, and after 4 weeks all the animals were using the limb in the locked position to support themselves during locomotion and other activity. The unoperated limbs and tail were not amputated in eight of these cases because it was found that if enough time was allowed

Fig. 8 Synchronized motion picture and action potential records of locomotion. — A. Action potentials from flexor muscles transposed to act as extensors. — S. Synchronizer. Each phase (every tenth phase indicated) corresponds to one motion picture frame taken at 16 per second. — T. Time, in 1/60 second. — Motion picture frames 13–24 (numbers of frames correspond to phase numbers of synchronizer) illustrate typical crutch-like use of straightly extended forelimb. Frames 33–36 and 42–44 include additional suspended phases of locomotor cycle for correlation with oscillogram. Note that the transposed flexors do not contract in supporting phase (e.g., 15–19; 24) but discharge only in the original flexor phase, when limb is lifted forward (e.g., 13; 20–22; 34–36; 42–43). (Limb blurred in pictures during rapid lifting movement.) Lengthened discharge, phases 27–32, indicates an interruption of progression; elbow caved in and rat paused to lift forebody with back musculature, meanwhile extending elbow to position shown in frame 33. — Records taken 14½ months after operation.

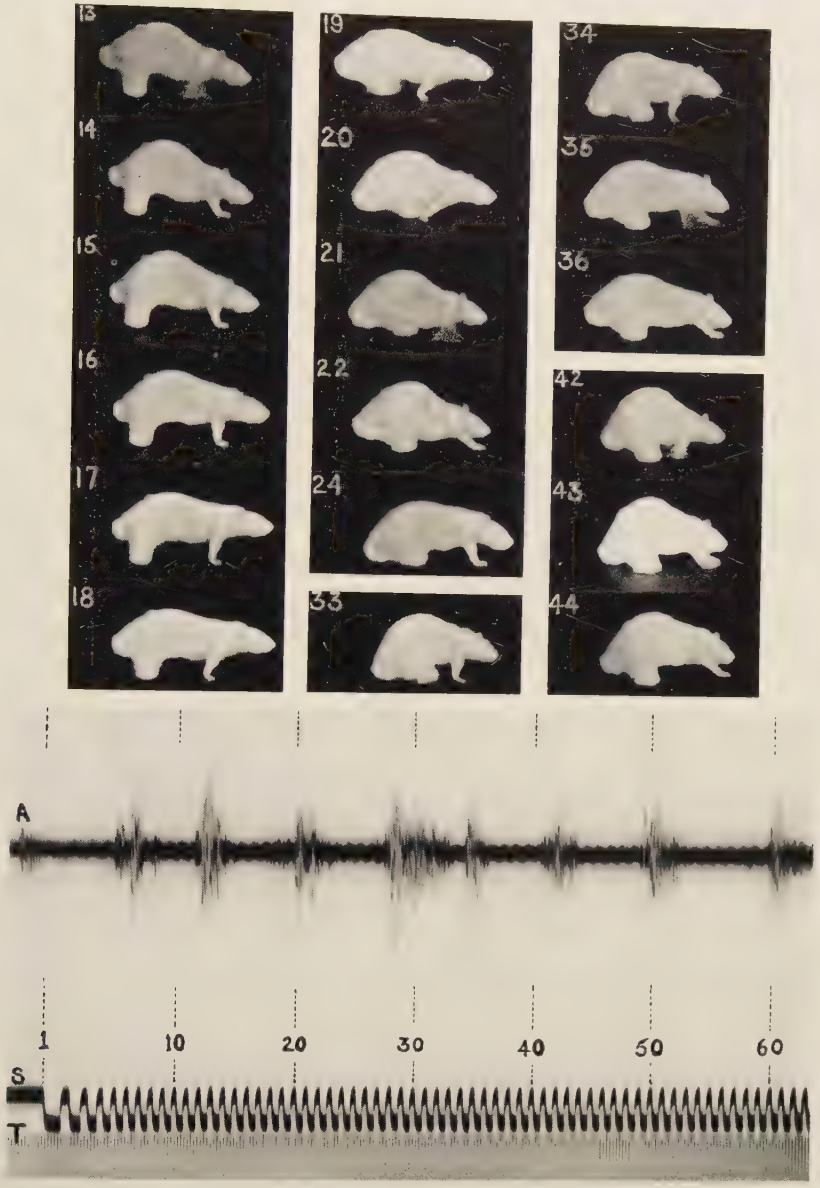
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Figure 8

after the operation, the rats used the limb sufficiently so that there could be no question but that they were actually supporting a good portion of the body weight upon it. In two cases the amputations were performed after 5 weeks as a matter of control. There was no essential difference in the action of the transposed muscles in the amputated and unamputated cases.

The biceps muscle supplied by the triceps nerve did not recover function until after the trick adjustment had become firmly established in all cases. When the biceps began to function it did not abolish or hinder the adjustment. In none of the rats did the biceps ever come to produce complete flexion of the elbow. After 2½ months, two of the rats were actively flexing the elbow about 105 degrees, one other about 90 degrees, two others somewhat less than that, and in the remaining three no overt active flexion could be distinguished for certain. On examination under anesthesia the biceps was found to be of full size in all ten animals. The nerve had regenerated and there was no sign of misregeneration. Electrical stimulation of the triceps nerve produced strong contraction of the biceps in all these cases as determined by change in shape of the muscle. The resting length of the biceps had been somewhat increased, however, and contraction of the muscle did not produce as complete flexion of the joint as does the normal biceps. Keeping the limb continuously in complete extension during the period of biceps paralysis had apparently stretched the biceps just as it had the triceps in the preceding series.

In two cases, 1½ months after operation, the tendons of the latissimus dorsi and pectoral muscles were cut bilaterally. As a result the test limb caved in whenever the animals leaned on it while the contralateral forelimb continued successfully to support the forebody. After bilateral severance of the tendons of the infraspinatus and deltoid muscles in another case the rat continued to use the test limb for support in the locked position and the contralateral forelimb in the normal position of partial extension.

Action potential analysis showed that in all cases the triceps nerve was activating the biceps muscle in the original extensor phase of coordination except when the joint was kept locked. Biceps contraction was inhibited in the locked joint reaction. During relapses of the locked joint adjustment the biceps contracted in the normal triceps phase of coordination. In those six cases in which biceps contraction produced overt flexion of the elbow in behavior, elbow flexion always occurred when extension occurs in normal and control animals and never in the normal flexor phase of activity. Thus these results generally corroborate those of the preceding section.

In addition the fact that the biceps innervated by triceps motor neurons did not, on recovery of function, hinder or abolish the locked joint reaction indicates that the adaptive inhibition of the triceps centers that occurred in both this and the preceding series did not constitute a specific adaptation in the action phase of the triceps motor neurons, but that the inhibition was rather a normal component of the shoulder movement involved in the trick adjustment. This interpretation was supported by action current analysis which showed in both series that when the elbow joint gave way and the triceps, or biceps supplied by the triceps nerve, contracted in its normal extensor phase, this contraction followed rather than preceded the caving in of the joint. Evidently in acquiring the new method of supporting themselves, the animals had relied entirely upon the motor patterns of the normal intact musculature and had made no specific corrections in the timing of the test muscles.

DISCUSSION

In most reactions the transposed muscles in these rats continued to contract when they would have contracted normally had the muscles not been transposed, and the muscles innervated by nerves of antagonistic muscles continued to contract in the normal action phase of the antagonistic muscles which the nerves had originally supplied. One exception to the resultant reversal of elbow movement was the maintenance

of elbow extension during supporting phases of coordination. This maintenance of extension was dependent upon the mechanical locking of the elbow joint and upon the action of shoulder rather than test muscles and hence has been referred to as a "trick" adjustment. It appeared abruptly, instead of being acquired by trial and error. The adjustment never appeared when the elbow was prevented from locking in the supporting phase of movement by a partial ankylosis of the joint or by either the action of the transposed triceps muscle or by severance of the tendons of adductor muscles of the shoulder. The degree of improvement in time was relatively slight. In no case did the trick adjustment ever become so well controlled that relapses were not common. When the elbow was prevented by a peg from locking in animals that had been using the trick adjustment for as long as 9 months, the forelimb was rendered uselss as a means of support. Cutting the tendons of the adductor muscles of the shoulder after 12 months abolished the ability to use the limb for support. In the adjustment the flexor motor neurons supplying the test muscles continued to the end to discharge in their normal flexor action phase instead of shifting their timing to suit the postoperative conditions. There was an inhibition of the transposed extensors as well as flexors supplied by extensor nerves during the adjustment, but whenever these muscles did work, they contracted in the original extensor phase of movement. This inhibition of the extensor motor neurons whenever the adjustment was used was evidently a normal part of the adductor movement of the shoulder used in the trick adjustment, instead of a specific correction in the timing of the extensor centers. When one flexor muscle was transposed and another left in position to oppose it, there was no adjustment in the action of either muscle. They continued to function synchronously although experimentally they had been made into anatomical antagonists.

The mechanical locking of the elbow joint, which made it possible for the rats to support themselves on the operated limb, furnished an excellent starting posture for learning to

correct the reversed action of the elbow. Progression from the mechanical support to maintaining the joint more firmly in the extended locked position by contraction of the test muscles and finally to maintaining extension by the action of the test muscles alone and controlling the degree of extension by the intensity of their contraction, should have been easy successive steps in reeducation. The rats, however, after months of practice in which they were forced by amputations to use the operated limb continually, never learned to activate the flexor centers during the normal extensor phase of activity so as to use the forelimb in normal manner. Instead, the flexor centers continued to fire in their original innate action phase, and the animals remained permanently dependent on the unreliable and awkward mechanical support.

These experiments fail to reveal any essential difference between the forelimb and the hind limb with respect to the modifiability of the basic coordination patterns. The trick adjustment which appeared in these experiments furnished a set of favorable cues for reeducation that was absent in the hind limb experiments where no such favorable response occurred and the sensory cues for reeducation had to come entirely from unfavorable reversed movements. Also in the case of these forelimb experiments the reversed action of the test muscles produced a greater dissolution of the normal array of those proprioceptive stimuli from the rest of the limb segments that tend to reinforce the normal function of the test muscles. Both these factors increased the chances for readjustment in the forelimb. The fact that no corrective adjustment in the timing of the test muscles occurred in spite of the more favorable conditions, indicates that the basic motor patterns for forelimb as well as for hind limb coordination in the rat are too firmly established to be broken down and remolded to suit these experimental reversals of the motor periphery.

The stability of these normal coordination patterns suggests an inherited rather than an acquired basis. Some of the animals in these experiments could have had no more than

25 days including intra-uterine practice to acquire the normal coordination patterns whereas they failed for 15 months to develop new reversed patterns suited to the postoperative conditions. The age of maximum learning capacity of the rat is well beyond the stage at which the animals were operated (Liu, '28). These results, in line with similar data obtained on lower vertebrates (Weiss, '41 b), indicate that the central organizing mechanisms underlying the normal basic motor patterns in the rat are in large part inherited rather than acquired by experience.

The trick adjustment that appeared in these animals may be considered somewhat similar to those adaptations in coordination that follow the loss of limbs in mammals (see Bethe and Fischer, '31). Such adaptations involve coordination of the intact musculature which, although far from normal in superficial appearance, may be produced by mere quantitative modification and recombination of the basic motor patterns that, as units, remain qualitatively unmodified. In adjustment to limb amputations, the groups of closely related muscles in the remaining musculature must still function in their normal agonist-antagonist relations. Some elementary motor patterns are accentuated and others inhibited, but there is no necessity of directly reversing the action of individual muscles with respect to other muscles of the same functional group as there is after nerve crossing and muscle transposition. The trick adjustment, involving changes in the action of the intact musculature in adaptation to the abnormal elbow movement, enabled the rats to balance unsteadily on the straightly extended forelimb. However, the more basic form of adjustment that would have involved a reversal in timing of the test muscles themselves to restore the more effective, normal use of the elbow never appeared. This latter type of adjustment requires more drastic modification of the basic coordination patterns than do those adjustments that occur in an intact musculature.

The nervous system may be extremely plastic, as contended by Bethe, at the higher levels of organization. But the results

of these experiments support the interpretation of Brown ('14), Weiss ('41 b), and others that at the base of the hierarchial organization in the nervous system are motor patterns the functional integration of which is extremely unplastic. The nervous system, particularly in the lower motor centers, is not merely a plastic, homogeneous connecting network whose patterns of activity are organized solely by the incoming sensory stimuli, but contains stable organizing mechanisms of its own.

SUMMARY

1. In fifteen rats the long biceps and brachialis flexor muscles were transposed so that they acted as extensors of the elbow joint instead of flexors.

2. In seven rats the nerve of the biceps muscle was crossed into the long triceps extensor muscle so that this muscle was activated from the spinal centers by flexor instead of extensor motor neurons.

3. In nine cases the biceps flexor was left in normal position and the brachialis flexor was transposed to act as an extensor in antagonism to its normal co-flexor.

4. In fourteen cases the biceps and brachialis flexors were transposed to the extensor position and the long triceps extensor was transposed to act as a flexor.

5. In ten cases the long triceps nerve was crossed into the biceps muscle and the brachialis flexor was transposed to act as an extensor.

6. In all cases all brachial muscles acting on the elbow joint except the test muscles were excised. The great majority of cases were operated upon at ages under 40 days, the youngest ones at 15 days. In all but eight of the animals the contralateral forelimb, the ipsilateral hind foot, and tail were amputated shortly after the test muscles recovered function. The animals were kept under observation well over a year after the operations. Operated control animals were run throughout with the experimental groups.

7. In most reactions the motor neurons to the test muscles continued permanently to discharge in their original innate

action phase without adjustment to the reversed anatomical arrangement.

8. The one exception to the general resultant reversal of elbow movement was the maintenance of the elbow in an extended locked position during supporting phases of activity. The forelimb was kept straightly extended and used like a crutch for support. This constituted a "trick" adjustment in that it was accomplished by the action of the intact musculature of the shoulder plus a mechanical locking of the elbow joint rather than by a corrective adjustment in the action phase of the test muscles.

9. This awkward trick adjustment appeared abruptly without practice and furnished an excellent point of departure from which to begin reeducation. In spite of long training, however, the rats never learned to improve upon the clumsy and unreliable mechanical method of support by correcting the reversed function of the test muscles.

10. The experiments demonstrate the unplasticity of the basic motor patterns for forelimb coordination in the rat.

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